"USEFULNESS OF PULSE OXIMETRY AND ANKLE BRACHIAL INDEX FOR SCREENING ASYMPTOMATIC PERIPHERAL VASCULAR DISEASE IN TYPE 2 DIABETES MELLITUS"

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For the Award of the Degree of

M.D. (GENERAL MEDICINE) - BRANCH – I

GOVERNMENT KILPAUK MEDICAL COLLEGE

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MAY 2019

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This is to certify that "USEFULNESS OF PULSE OXIMETRY AND ANKLE BRACHIAL INDEX FOR SCREENING ASYMPTOMATIC PERIPHERAL VASCULAR DISEASE IN TYPE 2 DIABETES MELLITUS" is a bonafide work done by **Dr. A. S. NATH** Post graduate student, Department of General Medicine, Kilpauk Medical College, Chennai-10, under my guidance and supervision in partial fulfilment of rules and regulations of the Tamil Nadu Dr. M.G.R Medical University, for the award of M.D. Degree Branch I (General Medicine) during the academic period from MAY 2016 To MAY 2019.

PROF. DR. K.V. RAJALAKSHMI M.D.
Guide for the Study,
Professor and Head of the Department,
Department of Medicine,
Govt. Kilpauk Medical College,
Chennai – 600 010

PROF. DR P. VASANTHAMANI,
M. D., D.G.O., MNAMS
The DEAN
Govt. Kilpauk Medical College
Chennai - 600 010

DECLARATION

I solemnly declare that this dissertation **"USEFULNESS OF PULSE OXIMETRY AND ANKLE BRACHIAL INDEX FOR SCREENING SYMPTOMATIC PERIPHERAL VASCULAR DISEASE IN TYPE 2 DIABETES MELLITUS"** was prepared by me at Government Kilpauk Medical College and Hospital, Chennai, under the guidance and supervision of **Prof. Dr. K. V. RAJALAKSHMI M.D., FMMC,** Professor and Head of the Department, Department of General Medicine, Government Kilpauk Medical College and Hospital, Chennai. This dissertation is submitted to The Tamil Nadu Dr. M.G.R. Medical University, Chennai in partial fulfilment of the University regulations for the award of the degree of M.D. Branch I (General Medicine).

Place: Chennai-10 **Dr. A. S. NATH**

Date:

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Prof. Dr. K.V. RAJALAKSHMI M.D.
Guide for the study,
Professor and Head of the Department,
Department of Medicine,
Govt. Kilpauk Medical College,
Chennai.

Date :

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The Institutional Ethical Committee of Govt. Kilpauk Medical College, Chennai reviewed and discussed the application for approval "USEFULNESS OF PULSE OXIMETRY AND ANKLE – BRACHIAL INDEX FOR SCREENING ASYMPTOMATIC PERIPHERAL VASCULAR DISEASE IN TYPE 2 DIABETES MELLITUS" submitted by Dr.A.S.Nath, Post Graduate in General Medicine, Govt. Kilpauk Medical College, Chennai-10.

The Proposal is **APPROVED.**

The Institutional Ethical Committee expects to be informed about the progress of the study any Adverse Drug Reaction Occurring in the Course of the study any change in the protocol and patient information /informed consent and asks to be provided a copy of the final report.

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Govt. Kilpauk Medical College,
Chennai-10.

ME I Sec> Ethical Committee

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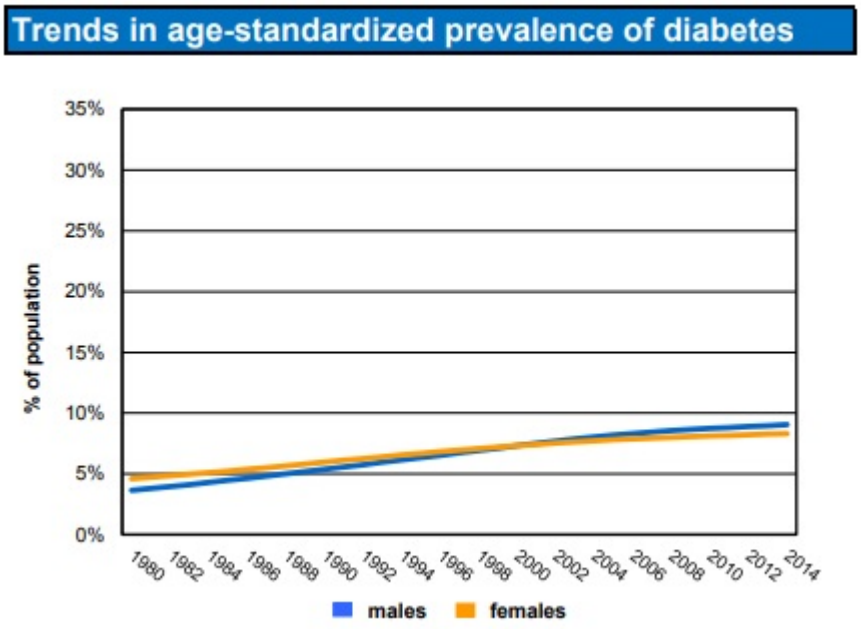
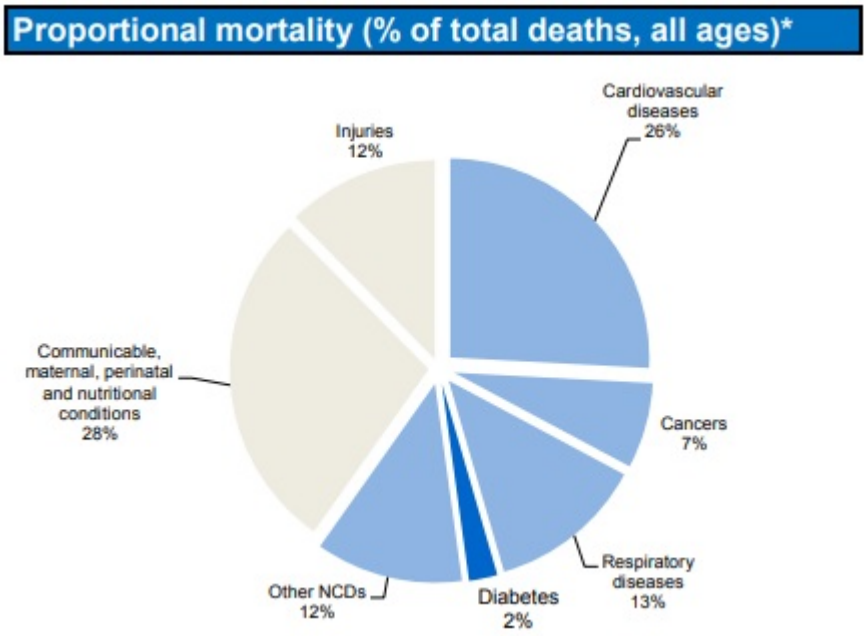
INTRODUCTION

According to the South East Asia Regional Office (SEARO) of the World Health Organisation (WHO) statistics, approximately 60 million Indians are living with the deadliest non-communicable disease of our times – DIABETES MELLITUS. It is estimated that 8.7 % of this population are between the ages 20 years and 70 years [1]. This denotes that 1 out of 9 individuals constituting the working force of our country are diabetics.



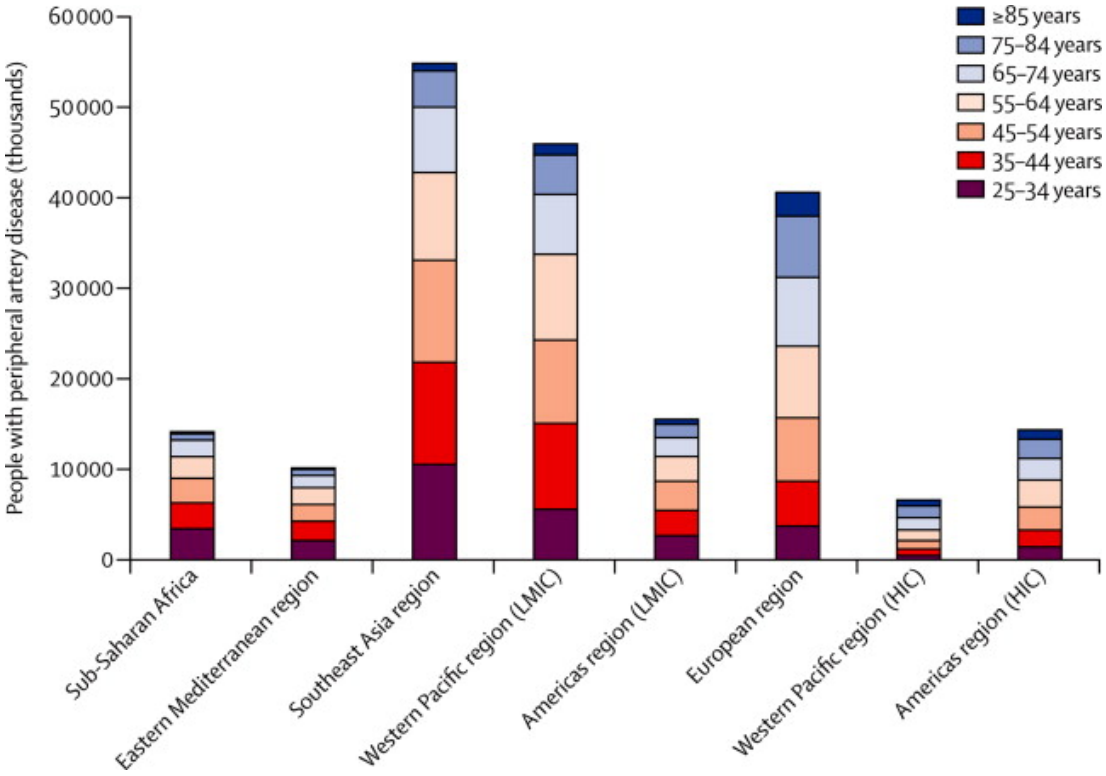
The appalling fact is that the same data sheet throws to light that around half of these people living with diabetes mellitus are undiagnosed, untreated or at best undertreated. This leads to poor glycemic control and hence earlier progression to both micro vascular as well as macro vascular complications of Diabetes mellitus.



The well recognised complications of Diabetes Mellitus – due to the injurious effects of hyperglycemia are generally separated into two categories[2]

1. Macro Vascular Complications
    a. Coronary Artery Disease
    b. Peripheral Vascular Disease
    c. Stroke
2. Micro Vascular Complications
    a. Diabetic nephropathy
    b. Diabetic neuropathy
    c. Diabetic retinopathy

The following graph adopted from The Lancet Updates shows the high prevalence of peripheral arterial disease in the South East Asian region compared to the Western population.



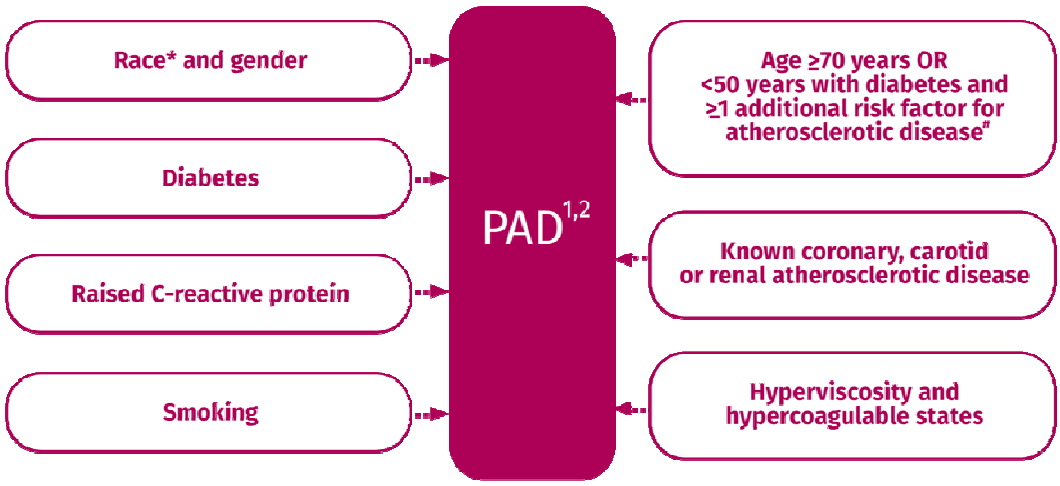
Various population based studies have been done in the past to assess the prevalence of Peripheral arterial disease in the Indian population and also to assess the prevalence of Peripheral arterial disease in patients with Diabetes mellitus.

Older studies like the Chennai Urban Population Study[3], reported the prevalence of Peripheral arterial disease in the diabetic population to be 6.3%. Perusal of more recent Indian studies [4],[5],[6] shows the prevalence of peripheral arterial disease in Diabetes mellitus to be increased. The cited research articles

show the prevalence of peripheral arterial disease in their diabetic populations to be 25.5%, 51% and 36% respectively.

The prevalence includes both symptomatic as well as asymptomatic diabetics with peripheral arterial disease. All the above studies defined Peripheral Arterial Disease as an Ankle Brachial Index < 0.9 and also confirmed through Colour Doppler Ultrasound.

The prevalence of Peripheral arterial disease in Diabetes mellitus has been consistently found to increase with age of the patient, duration of the diabetes mellitus and presence of other complications like diabetic neuropathy. This is in addition to the conventional risk factors for peripheral arterial disease such as physical inactivity, hypertension, smoking, deranged lipid profile et cetera.



PAD, peripheral artery disease

*More common in non-Hispanic black (7.8%) than white populations (4.4%), and slightly more common among males than females; [a]smoking hypertension, dyslipidaemia, hyperhomocysteinaemia

1. Hirsch AT *et al* - ACC/AHA PAD guidelines, *Circulation* 2006;113:e463-e654; 2. Norgren L *et al*, *J Vasc Surg* 2007;45:S5-S67

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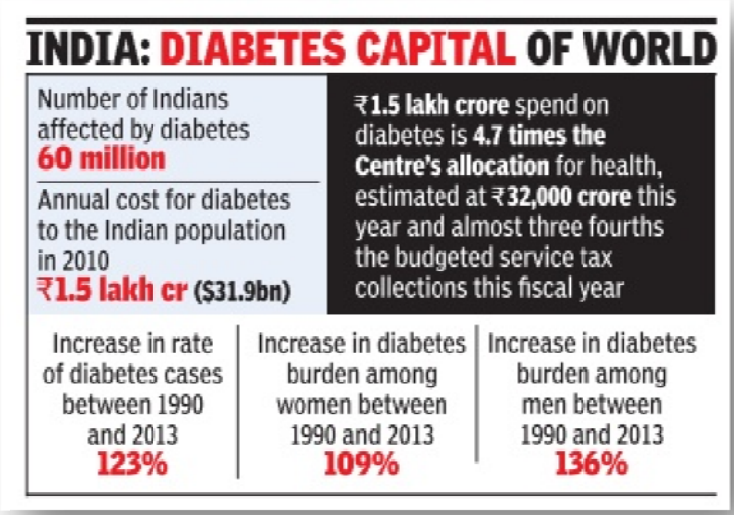
Peripheral arterial disease leads to significant morbidity and mortality in the Diabetic population due to the development of Diabetic Foot Syndrome. Diabetic Foot ulcers are the main clinical expression of Peripheral Arterial disease in diabetics. Diabetic Foot Syndrome is termed as a syndrome because the outcome of Diabetic foot ulcers[8] is deeply influenced by the co-morbidities present in the individual such as the presence of diabetic neuropathy, diabetic nephropathy, hypertension, heart disease et cetera. A recent study [7] conducted in a tertiary care hospital in Chennai reported the prevalence of Peripheral arterial disease in Diabetic Foot Ulcer to be 36%.

Around 30% of diabetics with Peripheral arterial disease require surgical or percutaneous endovascular revascularisation at some point during the course

of their disease. Furthermore, 10% of the diabetic population with peripheral arterial disease require amputation.

Diabetic Foot Syndrome not only significantly reduces the quality of life of the patient but also places a substantial economic burden on the health care system of the country [9]. The following graphic based on the studies conducted by the Institute for Health Metrics and Evaluation at the University of Washington in our country India in the year 2010 is testimony to the fact that diabetes mellitus and its complications need to be tacked effectively.



If Peripheral arterial disease can be picked up early, even before its clinical symptoms appear, then we may be able to prevent or postpone the occurrence of such complications as the Diabetic Foot Syndrome.

To this end many studies have been done to assess the usefulness of various tools to diagnose Peripheral arterial disease before the patient presents with the disease complication. The most widely studied tool is the Ankle

Brachial Index which has been proven to have a high sensitivity in diagnosing peripheral arterial disease.

The Ankle brachial index is measured using standard size sphygmomanometer cuffs and a handheld vascular Doppler probe of 8 hertz frequency. The detailed methodology is discussed later. However a handheld vascular probe is costly equipment not available with all medical personnel and also requires some amount of training to be used in the proper manner.

A cheaper and more commonly available tool that has been studied for its usefulness in detecting peripheral vascular disease is the finger pulse oximeter probe. The finger pulse oximeter combines spectrophotometry with optical plethysmography and has a reported sensitivity of more than 80% and specificity of 90% in detecting Peripheral arterial disease [10].

It is a cheap and simple tool which can be used at the grassroots level such as Primary Health Centres and Sub-Centres without any special training by medical as well as paramedical personnel alike.

There are not many studies which have aimed to test the usefulness of pulse oximetry as an independent tool in detecting peripheral arterial disease in asymptomatic individuals.

This vindicates the need for our study which aims to compare pulse oximetry with Ankle brachial index and test its power as an independent tool in detecting peripheral arterial disease and also to study the efficiency of these

tools in combination for the early detection of this deadly complication of Diabetes mellitus.

In this dissertation, the terms Peripheral arterial disease and Peripheral vascular disease have been interchangeably used.

AIMS AND OBJECTIVES

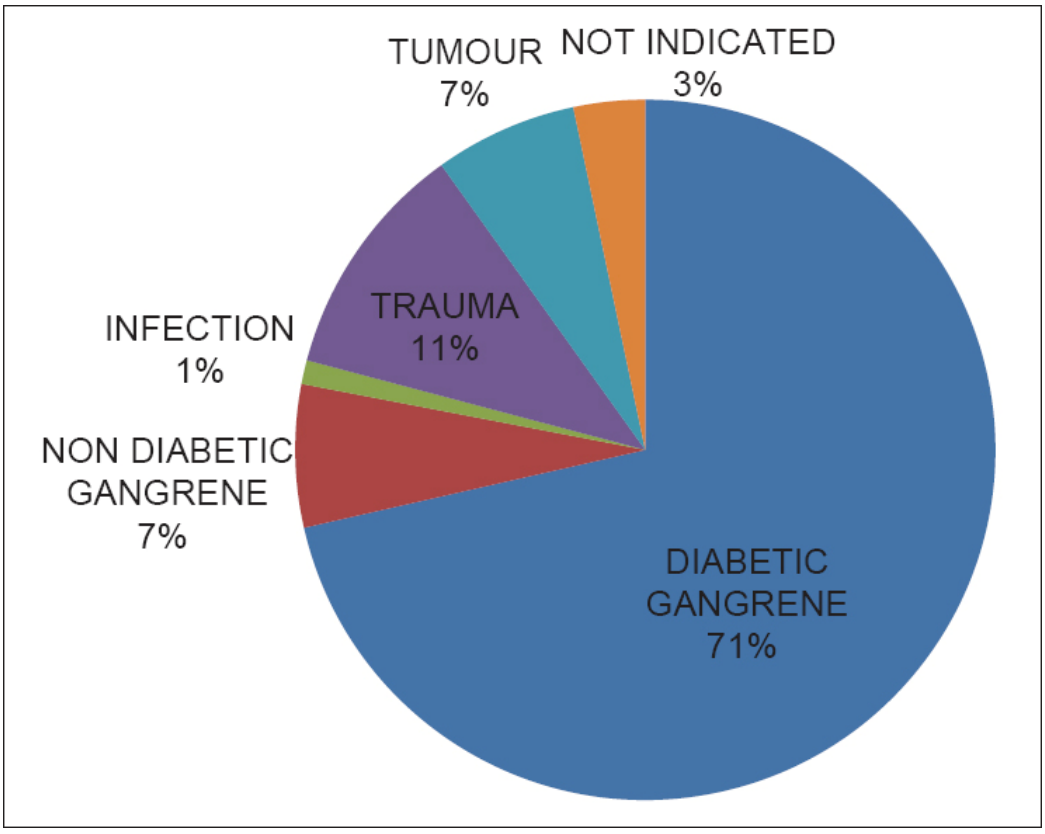
1. To assess the usefulness of Pulse oximetry in detecting Peripheral Vascular Disease in asymptomatic patients with diabetes mellitus.
2. To assess the usefulness of ABI in detecting PVD in asymptomatic patients with diabetes mellitus.
3. To compare these two index tests separately and in combination with a standard reference method - Duplex Ultrasonography of the Lower Limb arteries.

Pulse oximeter is a tool that is cheaper than all other modalities used to pick up Peripheral vascular disease. Positive results from this study can benefit the community by using Pulse oximeter for screening of all diabetic patients at regular intervals, even at the grassroots level by medical and paramedical personnel alike, to pick up Peripheral Vascular Disease at the earliest before clinical manifestations and occurrence of complications like Diabetic Foot Ulcer.

It will help to initiate appropriate therapy in those subset of patients with abnormal Pulse oximeter readings and a reduced Ankle brachial index after confirming the diagnosis through advanced modalities including Duplex ultrasonography and Peripheral Angiography.

REVIEW OF LITERATURE

Morbidity and mortality associated with Diabetes mellitus are largely due to the complications of the disease which affect many organ systems. Recent studies in our region are consistent with older studies that complications of diabetes mellitus including its vascular complications such as **Peripheral arterial disease** are the most common indication for major lower limb amputations [11].



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There is an interplay of many pathogenic factors which leads to increased incidence of foot ulcers and related morbidity in diabetic patients [12].

- Neuropathy
- Abnormal foot biomechanics
- **Peripheral arterial disease**
- Poor wound healing

A significant proportion of the patients who develop diabetic foot ulcers progress to need an amputation at some point or the other of their disease course. (14-24 % risk with that ulcer or subsequent ulcerations).

Factors that increase likelihood for development of foot ulcers and increase the risk of amputations include the following:

Male sex

Duration of diabetes mellitus > 10 years

Peripheral neuropathy

Abnormal structure of foot (bony abnormalities, callus, thickened nails)

Peripheral arterial disease

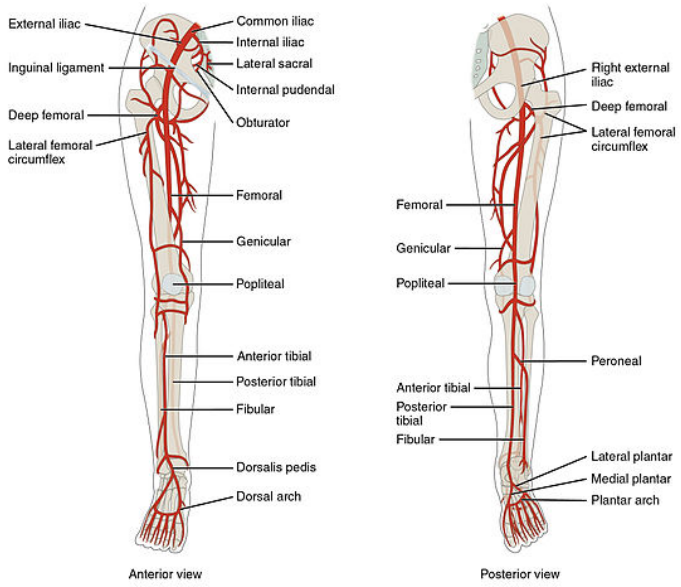
Smoking

History of previous ulcer or amputation

Visual impairment

Poor glycemic control

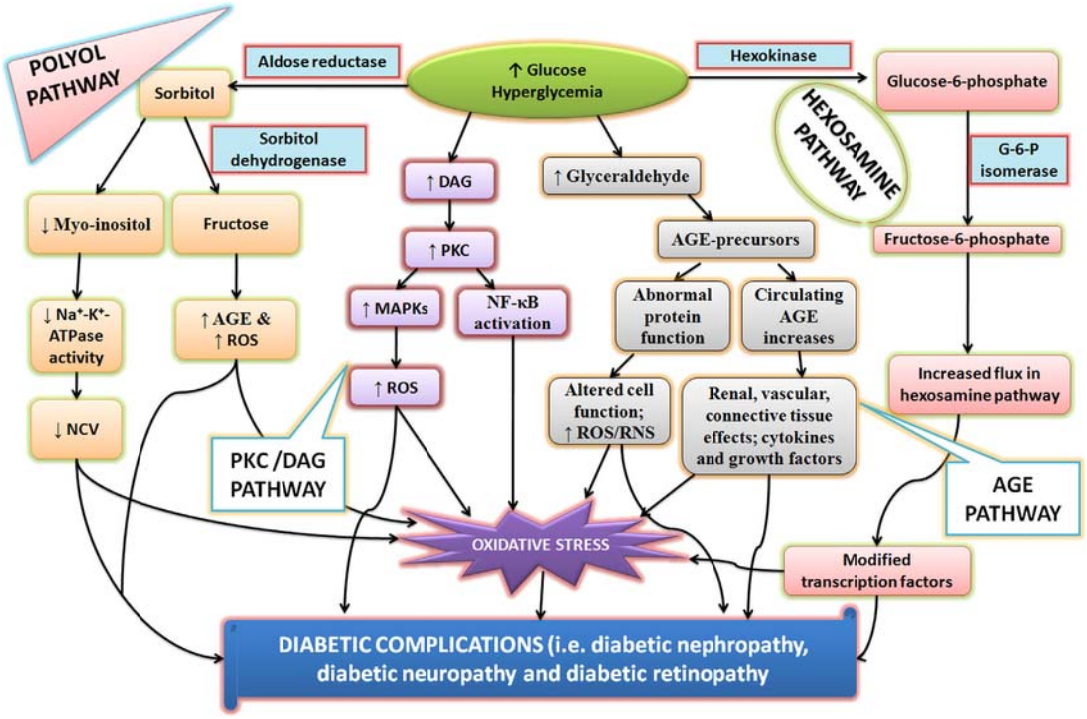
Diabetes mellitus increases the risk of development of peripheral arterial disease. While other conventional causes and risk factors promoting peripheral arterial disease involve the proximal musculature, peripheral arterial disease in diabetes mellitus tends to involve the distal vasculature more commonly – namely, the tibial and peroneal arteries.



However peripheral arterial disease in diabetes mellitus is multi-segmental and more extensive which portends a poorer progress than non-diabetic peripheral vascular disease. The other challenge associated with peripheral arterial disease diabetics is that the stenosis is slowly progressive and hence, the development of collaterals delays onset of symptoms leading to higher odds of delayed diagnosis. In the first place, fewer than 50% individuals with peripheral arterial disease are symptomatic [13].

Peripheral vascular disease in diabetes mellitus is also complicated by the occurrence of other complications like diabetic neuropathy and increased susceptibility to infections which leads to the Diabetic Foot Syndrome.

The theories on how hyperglycemia may be leading to chronic complications of diabetes mellitus are illustrated in the following flow diagram.



Increased concentration of glucose inside the cells leads to formation of large number of advanced glycosylation end products, which in the context of our discussion of peripheral arterial disease, leads to cross-linking of cell surface proteins via non-enzymatic glycosylation and causes endothelial dysfunction thereby promoting atherosclerosis.

Hyperglycemia also leads to increased accumulation of diacylglycerol, as shown in the diagram, which causes activation of Protein Kinase C. Protein Kinase C is responsible for alteration of transcription of genes for fibronectin,

Type IV collagen, contractile proteins, extracellular matrix proteins in endothelial cells and neurons.

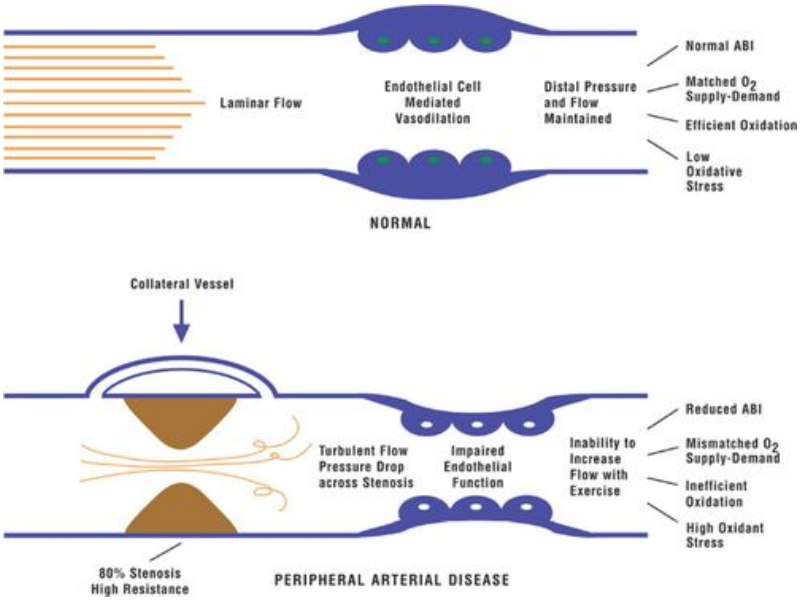
Increased flux of glucose through the hexosamine pathway generates increased amounts of fructose-6-phosphate, leading to altered function by glycosylation of proteins such as the endothelial nitric oxide synthase.

Other mechanisms are more apt to explain the pathogenesis of microvascular complications. Overall, strict glycemic control has been shown to reduce the incidence and progression of microvascular complications as evidenced by the United Kingdom Prospective Diabetes Study. Their influence on the occurrence and progression of macrovascular complications is less clear.

It is worthwhile to discuss regarding the hemodynamic changes occurring in Peripheral arterial disease.

Poiseuille first described these fundamental relationships by showing that flow was inversely proportional to the length of a tube, directly proportional to the pressure gradient, and directly proportional to the fourth power of the tube diameter [14].

Under normal conditions, flow is laminar and there is minimal pressure drop from the heart to the distal arterial circulation. However, with an arterial stenosis, there is a drop in pressure and flow across the stenosis. This pressure drop is accentuated by a loss of kinetic energy because of turbulent flow induced by the stenosis as shown in the figure below.



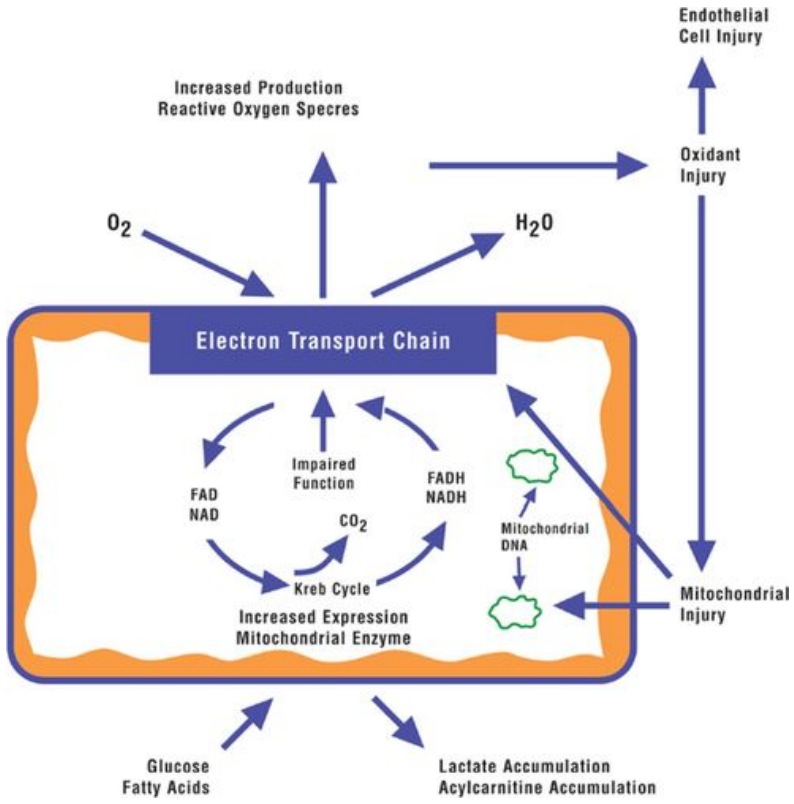
In the lower extremity, a series of arterial stenoses, for example, a stenosis or occlusion in the external iliac, superficial femoral arteries, and popliteal arteries, will be hemodynamically additive with the overall flow limitation of the sum of the individual components [15, 16]. These hemodynamic manifestations of PAD can be assessed with the ABI, which reflects the total hemodynamic burden of stenoses and occlusions from the central circulation to the ankle. Except for patients with noncompressible tibial vessels where the ABI does not reflect the intra-arterial pressure, patients with PAD will typically have an ABI <0.90 at rest.

In these scenarios, the toe brachial index can be useful.

Table 1. Mechanisms of Exercise Impairment in PAD

Healthy Physiology	PAD Pathophysiology
Arterial flow	Normal at rest, inadequate increment with exercise to meet metabolic demand
Endothelial and microvasculature dysfunction	Impaired endothelium-dependent vasodilation on exercise challenge
Inflammation	Increase in plasma levels of numerous inflammatory mediators; inflammation-impaired actions of progenitor/satellite cell differentiation and responses and growth factors
Reactive oxygen species and oxidative/reductive stress	During ischemia, skeletal muscle mitochondria release free radicals, including superoxide and other reactive oxygen species that are derived from the oxidation–reduction cascade
Muscle structural abnormalities	Muscle apoptosis and atrophy; fiber type switching; altered myosin heavy chain expression; fiber denervation
Muscle metabolic abnormalities	Altered oxygen coupling and mitochondrial respiration: in patients with PAD, prolongation of the kinetic rates of oxygen consumption, and tissue hemoglobin desaturation has been described at the onset of exercise

PAD indicates peripheral artery disease.



Peripheral arterial disease most commonly presents itself as intermittent claudication [13]. This is defined as a crampy pain or a sense of fatigue in the muscles. This ache or cramp is aggravated on exercise and relieved on taking rest. Femoro-popliteal disease manifests as claudication in the calf region whereas more proximal aorto-iliac involvement gives rise to pain in the buttock, hip and thigh.

With more severe stenosis, rest pain may develop. When resting blood flow is unable to meet the basal nutritional needs of the tissues, critical limb ischemia ensues. The classically described six Ps are seen then:

Pain on passive extension

Paraesthesia

Pulselessness

Pallor

Perishing cold

Paralysis

Physical examination findings of patients with Peripheral arterial disease include:

Decreased or absent pulses distal to the obstruction

Hair loss, smooth and shiny skin, reduced skin temperature

Pallor and/or cyanosis

Ulcers/ dry gangrene

Although a good history and a focussed physical examination are sufficient to diagnose peripheral arterial disease, an objective assessment to confirm the presence of the disease and ascertain its severity is obtained with the aid of non-invasive techniques.

A very useful clinical test that can be performed in the wards and has been extensively validated for its use in assessing functional status as well as response to treatment in a wide gamut of cardiopulmonary conditions including peripheral arterial disease is the 6-minute walk test [17].

Common conditions in which the 6 Minute Walk Test may provide useful information on response to therapy include:

1. Pulmonary arterial hypertension (PAH)
2. Heart failure (HF)
3. Cardiac rehabilitation/coronary artery disease (CAD)

Conditions where the 6 Minute Walk Test has been validated to be a significant predictor of morbidity and mortality include:

1. PAH
2. HF
3. **Peripheral arterial disease (PAD)**

Conditions where the 6 Minute Walk Test has been helpful for one time measurement of functional status include:

1. PAH
2. HF
3. CAD/cardiac rehabilitation
4. **Peripheral Arterial Disease**

Approximately one third of patients with Peripheral Arterial Disease who do not complain of exertional leg symptoms develop leg symptoms during the 6 Minute Walk Test. These individuals with "asymptomatic" Peripheral Arterial Disease who develop leg symptoms during the 6 Minute Walk Test presumably have lessened their physical activity to avoid exertional leg symptoms during their activities of daily living.

6 Minute Walk Test is reduced in patients with increasing severity of PAD. For example, in a single hospital study of PAD patients, 6 MWD by PAD severity was as follows: ABI <0.5: 290 m; ABI 0.5-0.7:312 m; and ABI

0.7-0.9:355 m. In the same dataset, patients in the lowest quartile of 6 MWD (<273 m) experienced two-fold increased risk of mortality over 4.8 years of follow-up when compared to patients in the highest quartile (>426 m) (HR 2.40; 95% CI; 1.32-4.38).

Six MWD at baseline was also shown to predict mobility loss in PAD patients. Supervised treadmill training increased 6 MWD in PAD patients by 35.9 m (95% CI; 15.3-56.5 m), whereas resistance training increased the 6 MWD by 12.4 m (95% CI; −8.42 to 33.3 m) when compared to a control group.

There are 2 existing classification systems for Peripheral arterial disease. One is the Fontaine system and the other is the Rutherford grading system which can be used to assess the severity of the Peripheral arterial disease.

This will help the treating physician to plan on appropriate pharmacotherapy, physical exercise rehabilitation and also referral to a vascular specialist for advanced imaging and planning of timely endovascular therapies.

FONTAINE		RUTHERFORD		
Stage	**Clinical**	**Grade**	**Category**	**Clinical**
I	Asymptomatic	0	0	Asymptomatic
IIa	Mild claudication	I	1	Mild claudication
IIb	Moderate–severe claudication	I	2	Moderate claudication
		I	3	Severe claudication
III	Ischemic rest pain	II	4	Ischemic rest pain
IV	Ulceration or gangrene	III	5	Minor tissue loss
		IV	6	Ulceration or gangrene

ANKLE BRACHIAL INDEX

The Ankle Brachial Index is a valuable tool to detect peripheral arterial disease. Normally, the systolic blood pressure in the upper and lower extremities is similar. Ankle pressure may be slightly higher than arm pressure due to pulse-wave amplification [13]. Therefore, in normal individuals, the Ankle: Brachial Index is 1.00 – 1.40. Ankle brachial index > 1.40 signifies vascular calcification and consequent non-compressible arteries.

With the development of hemodynamically significant stenoses, the systolic pressure in the leg is decreased and hence the Ankle Brachial Index starts to decrease. Values between 0.91 – 0.99 are considered borderline while values less than < 0.90 are deemed to be diagnostic of peripheral arterial disease.

The method to measure the systolic pressures in the arm and leg to calculate the Ankle Brachial Index is discussed under the Methodology section.

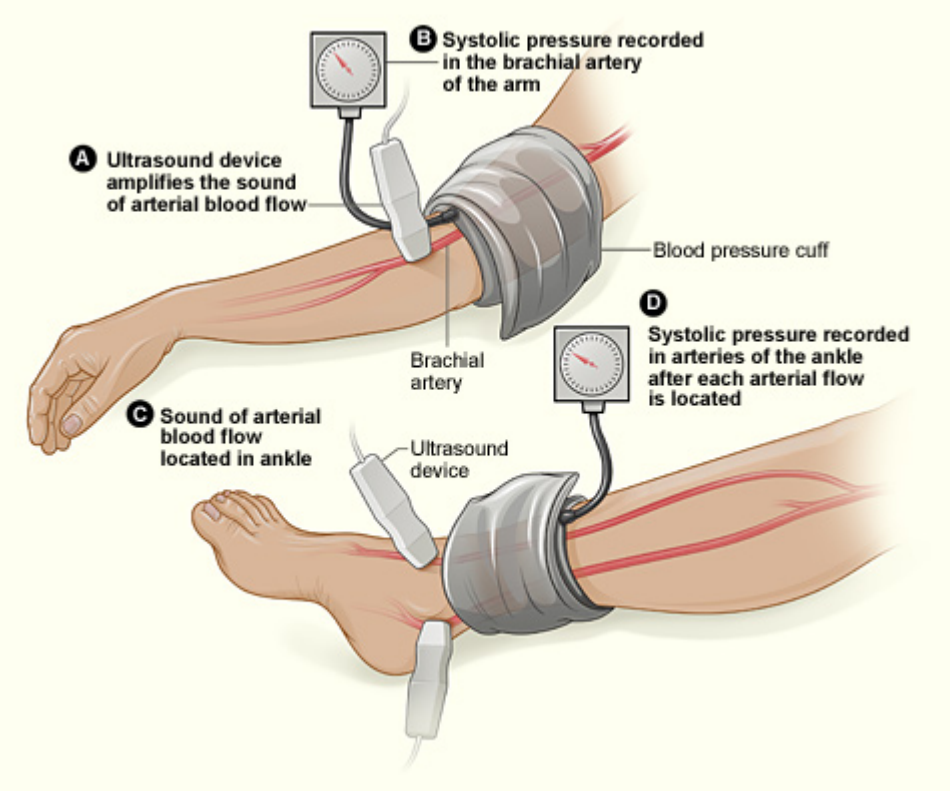
ABI Value	Interpretation	Recommendation
Greater than 1.4	Calcification / Vessel Hardening	Refer to vascular specialist
1.0 - 1.4	Normal	None
0.9 - 1.0	Acceptable	
0.8 - 0.9	Some Arterial Disease	Treat risk factors
0.5 - 0.8	Moderate Arterial Disease	Refer to vascular specialist
Less then 0.5	Severe Arterial Disease	Refer to vascular specialist

Stanford Medicine 25

Approximately 33% - 50% of patients with symptomatic Peripheral arterial disease have Coronary Artery Disease. Patients with Peripheral arterial disease have a 15 – 30 % 5-year mortality rate and a two- to six fold increased risk of death from coronary artery disease [13]. And hence a patient with peripheral arterial disease has greater probability of succumbing to the coronary artery disease than the peripheral arterial disease itself.

1-2 % of the patients with severe peripheral arterial disease progress to develop critical limb ischemia each year and a quarter of those patients require

amputation within one year. The prognosis is worse for patients who continue to smoke tobacco or have diabetes mellitus.



Ankle Brachial Index is the most recommended non-invasive screening test for Peripheral Arterial Disease. Recent publications have suggested that the interval between 0.9 and 1.10, considered as borderline - normal, may not be so [18]. Actually, an ABI ≤0.9 has been recommended by the American Heart Association [19]. Among well-trained technicians, its reliability has been excellent, and the validity of the test for stenosis of ≥50% in leg arteries is high (sensitivity of 90% and specificity of 98%) [20].

However, the sensitivity of the Ankle Brachial Index test varied widely among previous published studies. ABI detection in diabetes and the elderly

yielded lower sensitivity, 15 to 20%, 63%, 68%, 69.3% and 70.6%, suggesting that the test may be affected by diabetes status and aging.

And Feigelson et al. found that when they excluded patients with symptoms and signs of Peripheral Arterial Disease, Ankle Brachial Index values of less than 0.9 had a sensitivity of only 28.4%; and suggested that the Ankle Brachial Index seems less accurate as a screening test in patients without symptoms or signs of Peripheral Arterial Disease.

Though a recent publication in the Journal of the American Medical Association [14] of the United States Preventive Services Task Force also has expressed its reservations in the use of Ankle Brachial Index in the asymptomatic population, several studies conducted in many parts of our country India have repeatedly underlined the importance of the use of Ankle brachial index in the screening of peripheral arterial disease in both diabetic as well as non-diabetic populations.

Solanki et al. have studied PERIPHERAL ARTERIAL DISEASE in diabetics in an urban Indian population. Among the 110 diabetics included in their study, 46% had symptomatic PERIPHERAL ARTERIAL DISEASE and 35% had low Ankle brachial index [15].

Premalatha et al. conducted a larger study in urban South India. 1262 eligible subjects above the age of 20 participated. Oral glucose tolerance test was used to classify subjects into normal glucose tolerance, impaired glucose tolerance and diabetic. Prevalence of PERIPHERAL ARTERIAL

DISEASE in normal, impaired and diabetics is 2.7%, 2.9% and 6.3% respectively with overall being 3.2%. They found age over 50 years was a significant risk factor but observed no association with smoking.[16]

However ABI was measured in only 50% of subjects. This, in addition to the fact that this study was conducted in an urban area may explain the reports of low prevalence of PERIPHERAL ARTERIAL DISEASE in the study.

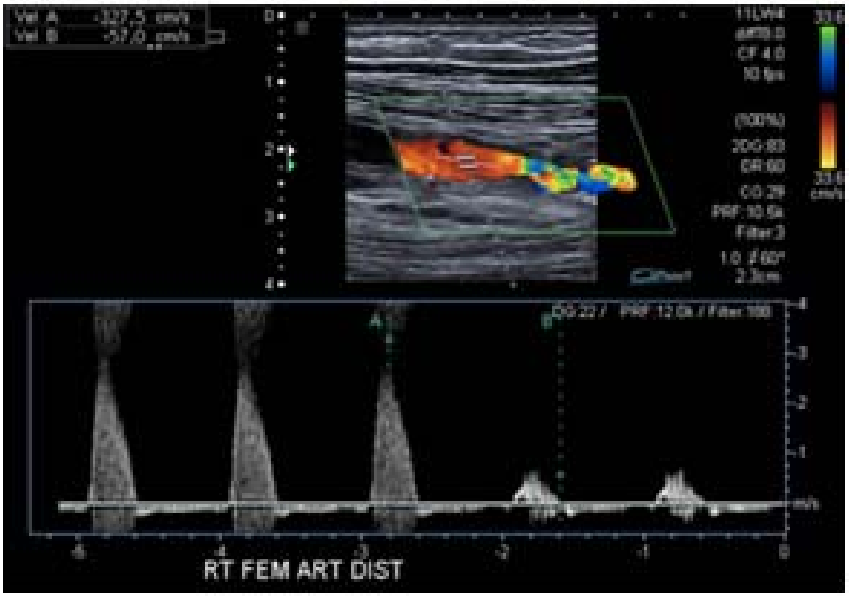
Sarangi et al. studied the correlation between PERIPHERAL ARTERIAL DISEASE and Coronary Artery Disease using Ankle Brachial Index in an inpatient setting in India. All patients were above the age of 45 years. Out of 182 patients only 32 (18%) had PERIPHERAL ARTERIAL DISEASE, of which 15 patients had Coronary Artery Disease.[21]

Khurana et al. showed prevalence of PERIPHERAL ARTERIAL DISEASE based on Ankle Brachial Index in Punjab, India. Out of the 200 diabetics with age >45 years, 33% had abnormal ABI $\leq$ 0.9.

Nag et al. in 2012 have published a study showing the association of chronic venous ulcer and peripheral arterial disease. They compared the Ankle Brachial Index and colour Doppler study for PERIPHERAL ARTERIAL DISEASE and found a strong correlation between them.[22]

DUPLEX SCAN

The other non invasive modality that has been used as the standard to diagnose Peripheral arterial disease in our study is Duplex ultrasonography which combines B-mode imaging and Doppler flow velocity waveform analysis examination [13].



Though conventional contrast angiography is considered the gold standard to diagnose Peripheral vascular disease [23], it is associated with significant morbidity in the form of radiation exposure, arterial puncture and risk of developing contrast induced nephropathy.

The peak systolic velocities (PSV) are used to identify stenotic vasculature. Duplex ultrasonography is useful to detect hemodynamically significant stenotic lesions in the lower limb peripheral arteries and has become an attractive alternative for the treatment planning of Peripheral Arterial Disease of the lower limb, now that many studies have vouched for its accuracy

[23]. Duplex Ultrasonography can be used as a guide to determine if percutaneous intervention is necessary [23].

PULSE OXIMETRY

Another non-invasive tool that has not been sufficiently validated is the finger pulse oximeter. Though some studies have concluded that pulse oximeter is comparable in efficacy to the Ankle brachial Index to detect peripheral artery disease in both the symptomatic and asymptomatic population, this tool has never been included in recommendations or guidelines issued by authorities.

The pulse oximeter is a simple and cheap tool and its potential may be harnessed in a limited resource setting like ours. The physical properties used in pulse oximetry are discussed below.

Pulse oximetry uses light to derive the value of oxygen saturation in the arterial blood of a person. Light is emitted from a light source such as a light emitting diode (LED) which beams across the pulse oximeter probe and reaches a light detector placed on the opposite side of the device.

When a finger is placed in between the light source and the light detector, the light will now have to travel through the substance of the finger to meet the detector. While a portion of the light will be absorbed by the finger, the portion of light rays which are not absorbed by the finger reaches the light detector.

The proportion of light which is absorbed by a finger is dependent on several physical properties and these parameters are made use of by the pulse oximeter to calculate the oxygen saturation.

The amount of light absorbed hinges on the following factors:

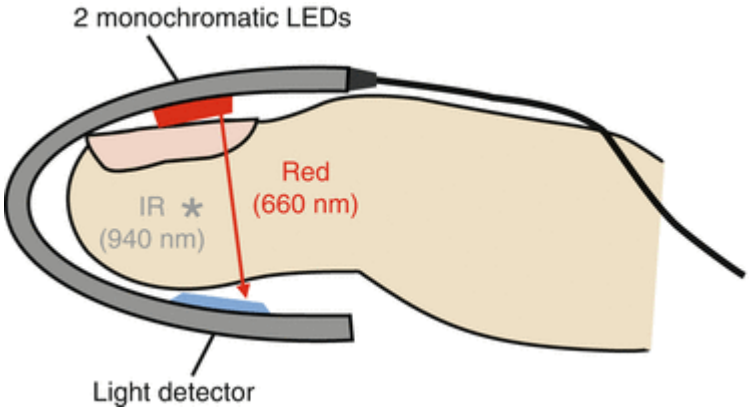
1. Concentration of the light absorbing substance.

2. Length of the light path in the absorbing substance.

3. Oxyhemoglobin and Deoxyhemoglobin absorbs red and infrared light differently

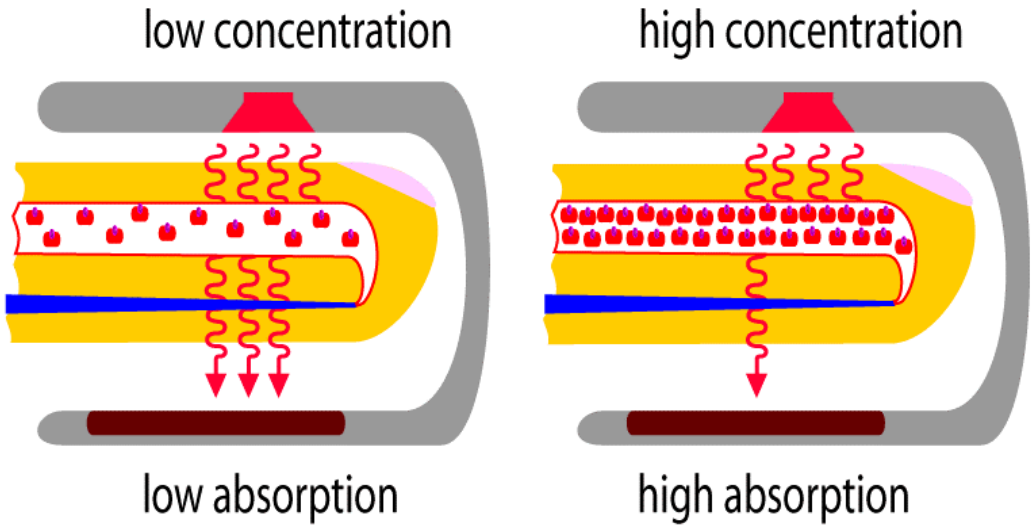
Concentration of the light absorbing substance:

The physical properties that a pulse oximeter uses are explained below. A finger is inserted into the probe. Above the finger are two monochromatic Light Emitting Diodes {LEDs} which act as the light sources that are emitting light. Inside the finger is a pulsatile artery which carries the blood the pulse oximeter is targeting to detect and derive the percentage saturation of oxygen in and a vein through which the blood exits the finger. Beneath the finger, a light detector is placed.



Haemoglobin absorbs light. The quantum of light which is absorbed is directly proportional to the concentration of haemoglobin in the blood.

In the diagram below, the blood columns in the two fingers have one and the same diameter. Albeit, one blood vessel has a low haemoglobin concentration (that is reduced number of haemoglobin units in each unit volume of blood) and the juxtaposed blood column has a higher Haemoglobin concentration (that is a high number of haemoglobin units in each unit volume of blood).



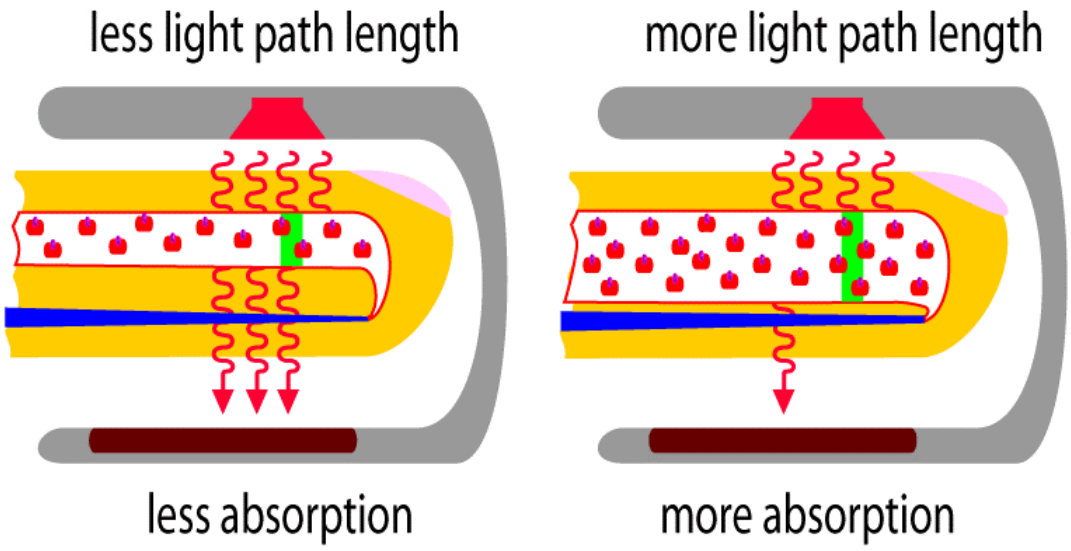
Every haemoglobin unit absorbs some of the light, so greater the haemoglobin per unit of area, more the light is absorbed. This property is otherwise described in physics as Beer's Law.

Beer's Law: Amount of light absorbed is proportional to the concentration of the solution.

By detecting the quantum of light which reaches the light detector, the pulse oximeter knows how much light has been absorbed. Higher the haemoglobin in the finger, more light is absorbed.

Length of the light path in the absorbing substance:

Two fingers are shown below. Both the arteries have the same concentration (similar haemoglobin concentration per unit area). The artery depicted on the right side is wider than the artery on the left.



The light emitted from the light emitting diode source has to travel across the artery. The light beam traverses a shorter course in the narrower

artery and has to beam through a longer path in the wider artery (paths are shown as green lines).

Though the concentration of haemoglobin is identical in both the blood columns, the light meets more haemoglobin in the wider artery because it travels a longer path. Therefore, longer the path the light has to traverse more is the light absorbed. This property is described in physics as Lambert's Law.

Lambert's Law: Amount of light absorbed is proportional to the length of the path that the light has to travel in the absorbing substance.

Oxy-haemoglobin and de-oxy-haemoglobin absorbs red light and infrared light differently:

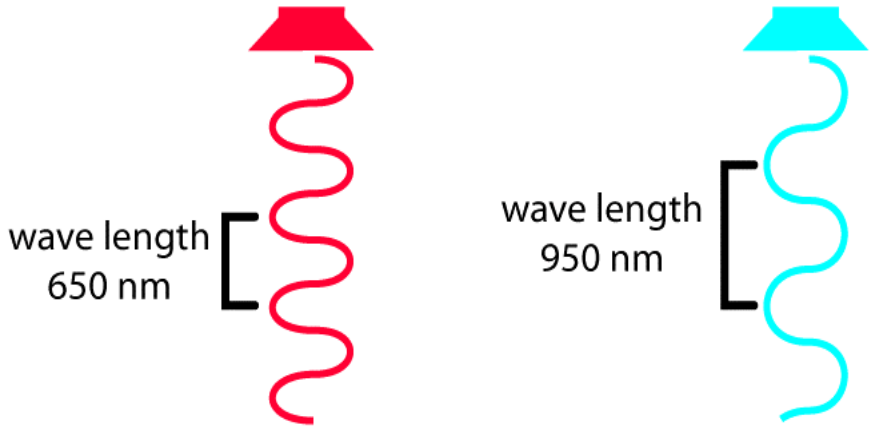
Oxy-haemoglobin absorbs more infrared light compared to red light whereas de-oxy-haemoglobin absorbs more red light as compared to infrared light.

The pulse oximeter makes use of this important property to calculate oxygen saturation. That is, oxy haemoglobin and de-oxy haemoglobin differ in their physical properties and hence absorb light of different wavelengths in specific ways.

The pulse oximeter uses lights of two different wavelengths to analyze haemoglobin:

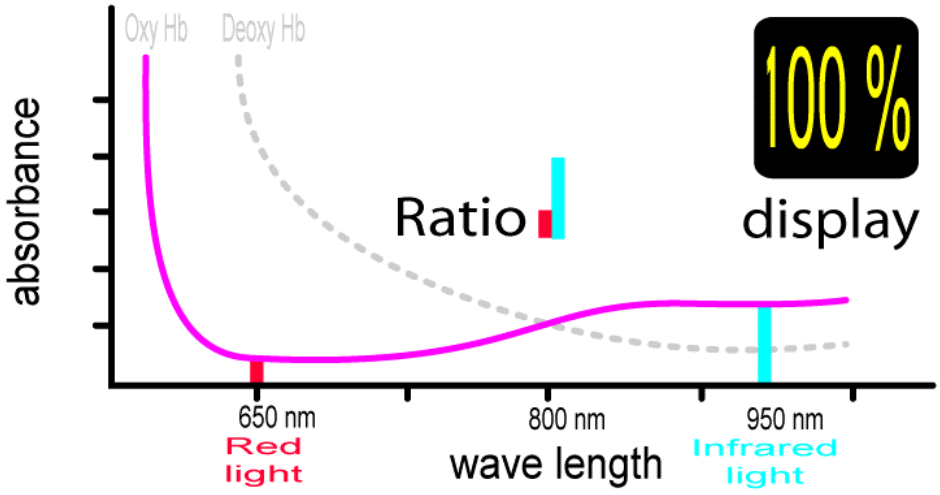
1. A red light with a wavelength of approximately 650 nm
2. An infrared light which has a wavelength of 950 nm

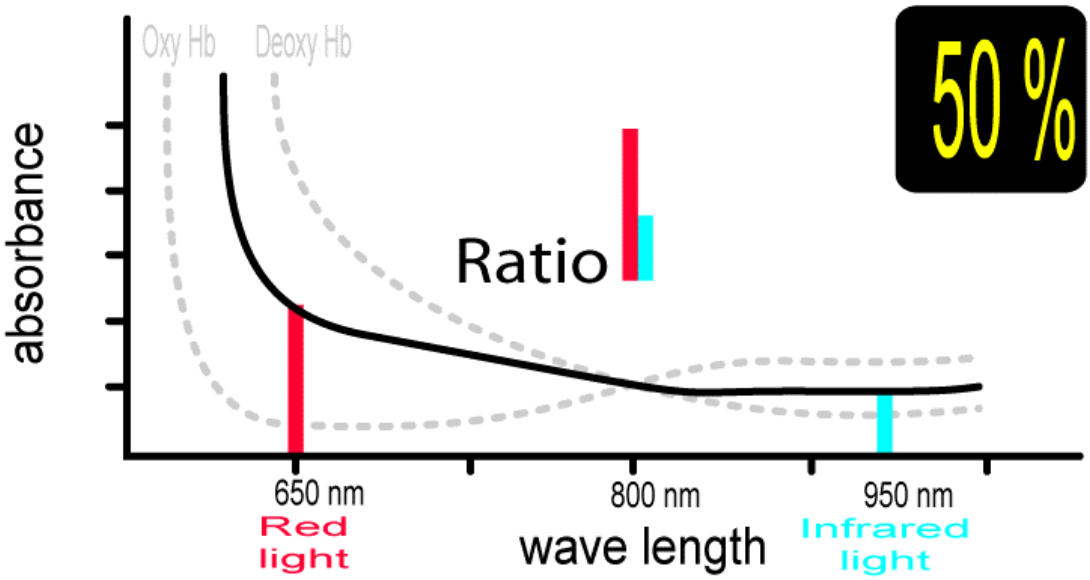
For pictorial representation purpose, the infrared light of 950 nanometer wave length is depicted in blue colour. In reality however, infrared light is invisible to the human eye.

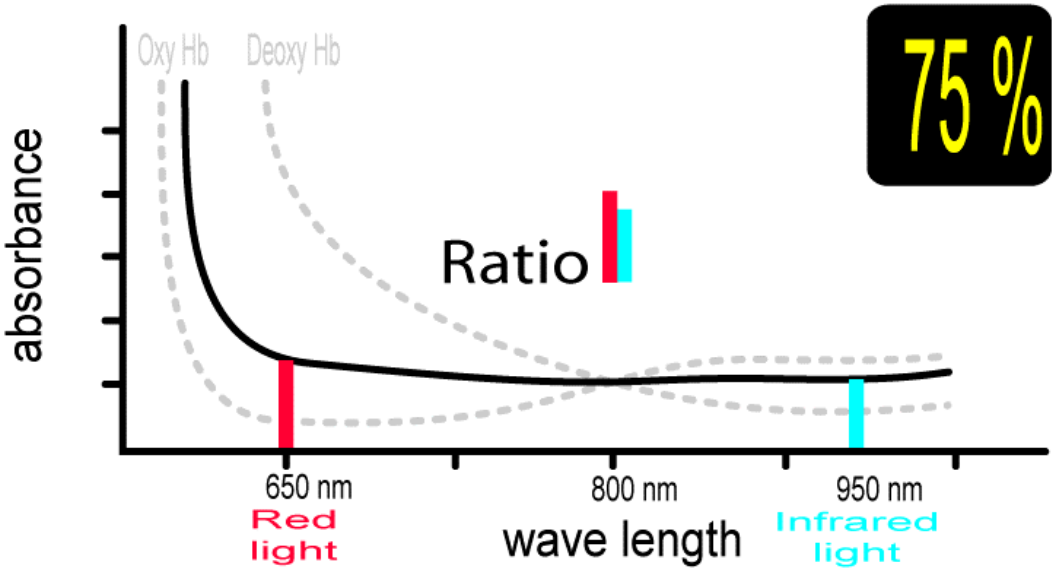


The pulse oximeter calculates the oxygen saturation by comparing the amounts of red light and infra red light that is absorbed by the blood column. Depending on the concentrations of oxy haemoglobin and de-oxy haemoglobin present, the ratio of the quantum of red light absorbed in comparison with the amount of infrared light absorbed changes.

Using this ratio, the pulse oximeter can then derive the oxygen saturation.

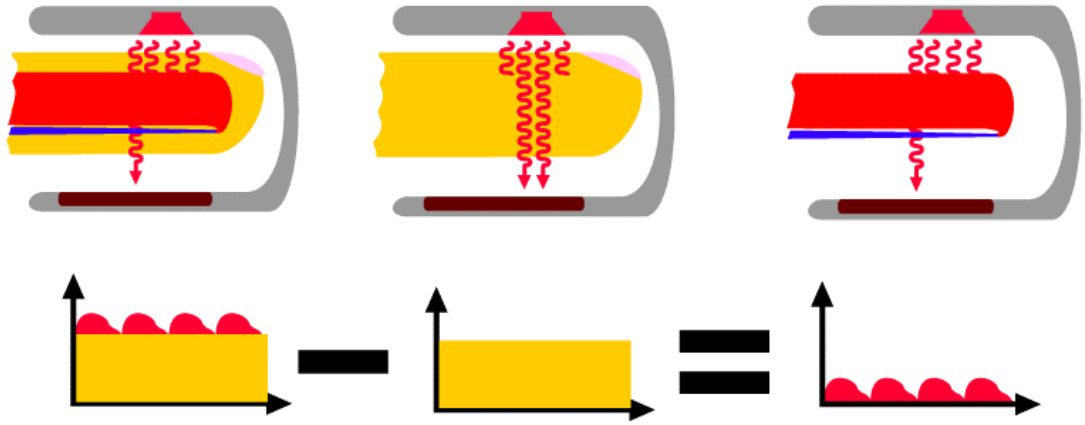



Oxy Hb
Deoxy Hb
50 %
absorbance
Ratio
650 nm
Red
light
800 nm
wave length
950 nm
Infrared
light


Oxy Hb
Deoxy Hb
75 %
absorbance
Ratio
650 nm
Red
light
800 nm
wave length
950 nm
Infrared
light

The blood column in the arterial vessel is not the only light absorbing substance in the path of the light rays from the pulse oximeter. The skin and the surrounding tissues also absorb some light.

The pulse oximeter circumvents this problem by using the concept of 'changing absorbance'. As shown below, the computer deducts the non-changing part of the absorbance signal from the total signal. After the subtraction, only the "changing absorbance signal" will remain, and this corresponds to the pulsatile arterial blood. In this way, the pulse oximeter calculates the oxygen saturation in arterial blood while filtering the effects of the surrounding tissues.



Review of studies which included Pulse oximetry:

It is a known fact that pulse oximetry measures peripheral blood haemoglobin oxygen saturation {SpO_2}. Low blood flow in the extremity produces lower SpO_2 in the blood, a fact that the vascular surgeons have been using to assess patency of arterial reconstructions.

Joyce et al. compared the Ankle Brachial Index, pulse oximetry spectrophotometry measurement in the toes, and trans-cutaneous oxygen tension readings with the arteriographic appearance in patients suspected of having limb ischemia. They found that pulse oximetry correlated best with the arteriographic appearance.

Jawahar et al. [24] studied patients between suspected Peripheral Arterial Disease group and non-suspected Peripheral Arterial Disease group. Pulse oximetry results were defined as abnormal if there was a reduction of greater than 2% in saturation in the toes from the fingers or a reduction of more than 2% on elevation of the foot by 12 inches.

While Pulse oximetry is a proven method for non-invasive evaluation of arterial oxygenation, there is considerably less number of studies that have validated its use in the detection of peripheral arterial disease.

A large repertoire of research material have established that pulse oximetry is accurate and reliable for screening of hepatopulmonary syndrome in which there is a typical finding of orthodeoxia, congenital heart disease, diabetes mellitus and sepsis .

Perhaps the first study which explored the possibility of using the pulse oximeter along with Ankle brachial index was done way back in 2005 by Iyer Parameswaran et al. [25] which yielded positive result in the sense that Pulse oximeter was looked at upon as a valuable aid to the surgeon's armamentarium to detect peripheral arterial disease in the suspected population.

The results of that study came to a conclusion that pulse oximetry was at least as accurate as Ankle Brachial Index and was an effective added method for screening patients with type 2 diabetes mellitus for Lower Extremity Arterial Disease.

Further comments were added that pulse oximeters are widely available in patient care areas and simple to use without any advanced training. The technique of measuring SpO_2 in the blood of the fingers, using a pulse oximeter, can be implemented with relative ease since it is well described and well known.

The application of the finger pulse oximeter probe to the toes of the feet does not differ from that with its application a finger. On an average, it took five minutes to finish the test. However, the study by Iyer Parameswaran et al. did not test for inter-observer variability of the finger pulse oximeter test.

A more recent study which tested the efficiency of the pulse oximeter in detecting peripheral arterial disease was done by Sateesh Kumar et al [26]. in the year 2012.

This study included diabetic patients from the out-patient department in a tertiary care centre. The prevalence of asymptomatic peripheral arterial disease in the diabetic population was found to be 22.5 %.

Pulse oximetry was found to be 74.1% sensitive and 95.7% specific for detection of peripheral arterial disease. When combined with the ankle brachial index, the sensitivity increased to 92.2 % and the specificity increased to 83.3%.

The study concluded that for asymptomatic individuals, pulse oximetry performed at least as good as Ankle Brachial Index if not better and the combination of the two modalities could be used as an efficient screening strategy for the diagnosis of asymptomatic Peripheral Vascular Disease among the diabetic population.

MATERIALS AND METHODS

Study design : Cross-sectional observational study

Study period : 6 months

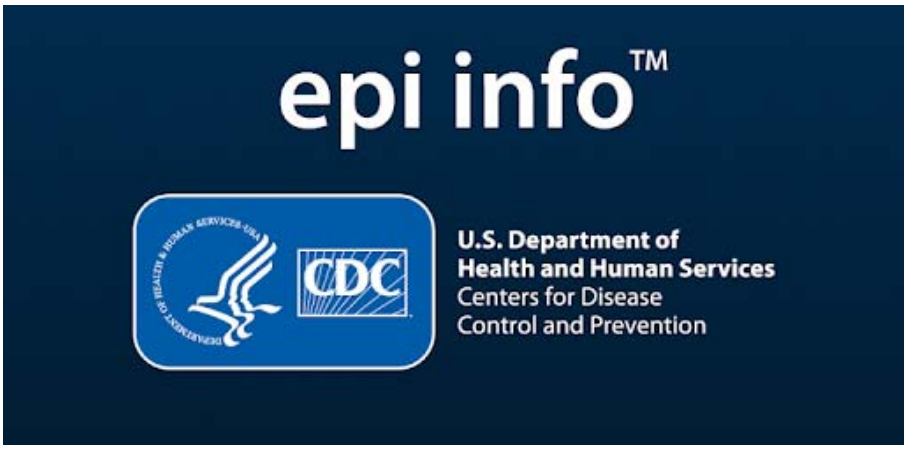
Study area : Government Kilpauk Medical College Hospital, Chennai

Study population : Patients with Diabetes Mellitus attending the Medicine / Diabetology Out-Patients departments at our tertiary care centre and In-Patients with Diabetes mellitus fulfilling inclusion criteria.

Sample size : 150

SAMPLE SIZE

- Sample size was calculated using the EpiInfo Application issued by the Center for Disease Control, America.
- The expected frequency of PVD in Diabetic patients in previous studies averages to 10%. Assuming 10% as expected frequency with 5% MOE and 95% Confidence level, the total sample size is 138. Assuming a non response rate of 10%, the final sample size is decided as 150.



INCLUSION CRITERIA

- Adults > 30 years of age pre diagnosed with Diabetes as per American Diabetes Association criteria, irrespective of duration of diabetes, glycemic control or presence of complications.
- Not previously diagnosed with Peripheral Vascular Disease and asymptomatic with regards to symptoms of Peripheral Vascular Disease such as claudication pain, swelling, ulcers, gangrene or previous history of amputations

EXCLUSION CRITERIA

- Age less than 30 years
- Any significant prior medical history of hyper-coagulable states, congestive heart failure, suspected arteritis or collagen vascular diseases.
- Patients who are unable to lie supine during the period of testing.
- Patients who are extremely sick requiring care in intensive care units.

CASE DEFINITION

By Duplex ultrasonography:

Monophasic flow in any one of the lower limb arteries is considered diagnostic of peripheral arterial disease.

By Ankle brachial index:

Ankle brachial index value less than 0.9 is considered diagnostic of peripheral arterial disease.

By Finger pulse oximetry:

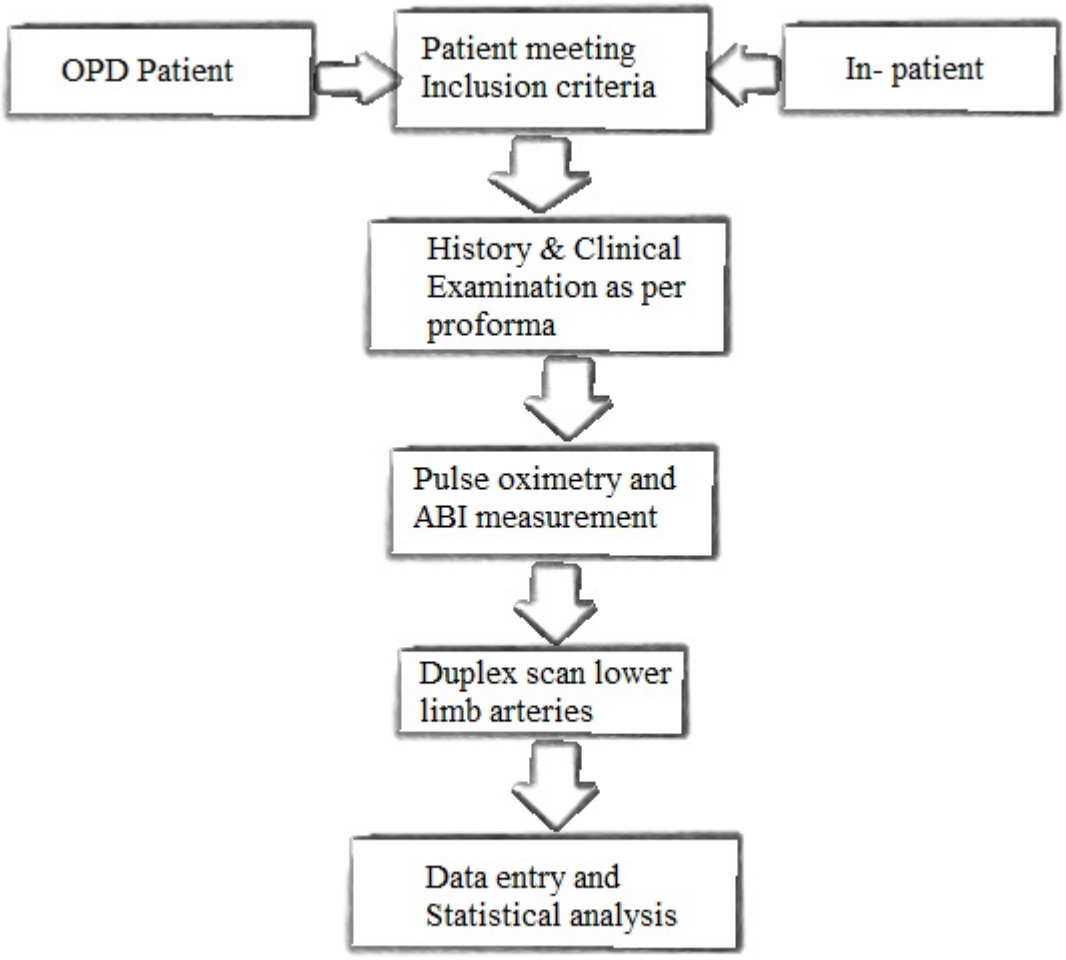
A saturation percentage of Oxygen {SpO_2 } value of more than 2% lower than the finger value or a decrease of more than 2% on elevation of the leg (decrease from the value at the supine position) [xx]

MATERIALS

- Patient information sheets in vernacular language
- Patient consent form in vernacular language
- Printed proformas
- Finger pulse oximeter
- 8 hertz handheld vascular Doppler
- Duplex ultrasonography machine

METHODOLOGY

This study is a cross sectional observational study conducted in our tertiary care hospital Government Kilpauk Medical College Hospital, Chennai. The duration of the study was six months. All the In-patients with diabetes mellitus and Out-patients with diabetes mellitus attending the Medicine and Diabetology Out-patient departments were screened for meeting the inclusion criteria.



The patients meeting the inclusion criteria were explained in detail regarding the nature of the study and its importance was emphasised. Each patient was given an information sheet regarding the study in the vernacular language. The patients were enrolled in the study after duly obtaining their informed written consent in the consent form.

A thorough medical history and clinical examination was done as per the proforma for each patient to ensure correct candidacy and whether they can be enrolled in the study as per the inclusion criteria.

The outpatients who were included in this study were first made to lie comfortably in supine posture on the examination couch of the examination room in the Medicine out-patient department. Finger pulse oximeter was applied first to the right index finger and the left index finger of the patient and the readings noted. This was immediately followed by recording the percentage of oxygen saturation readings in the right great toe and left great toe.

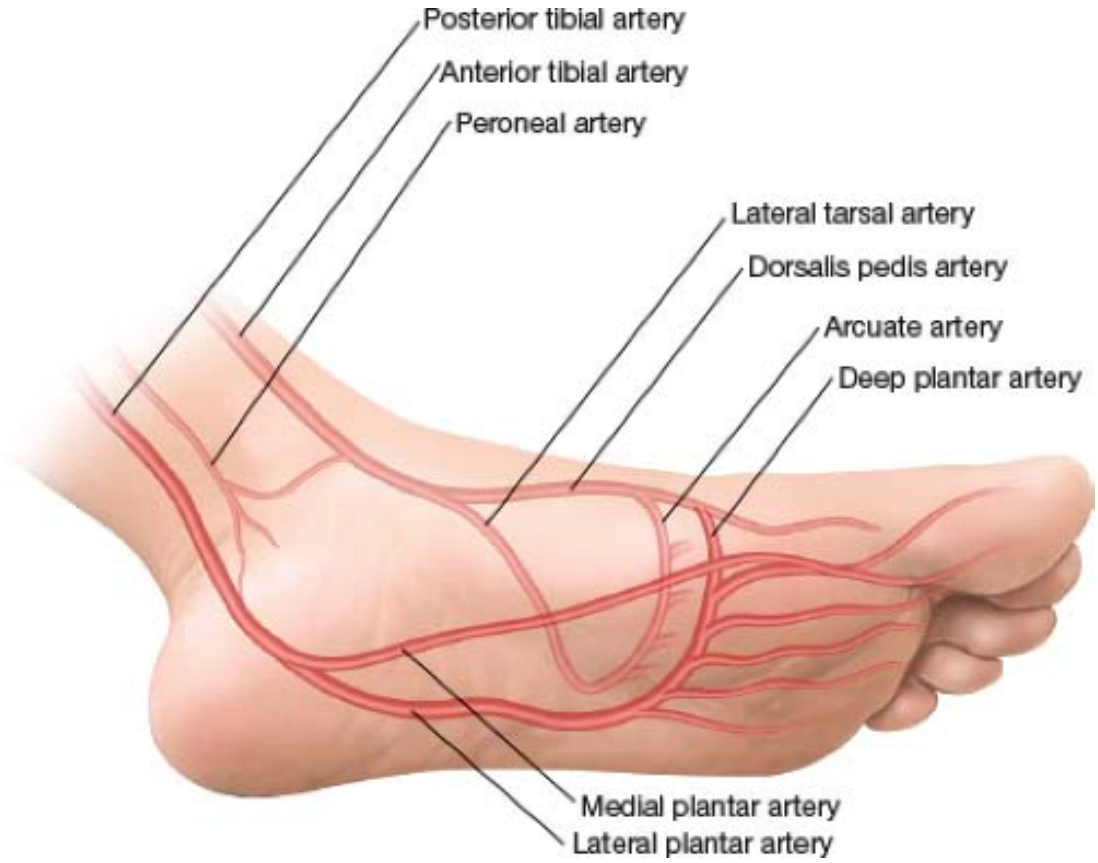
In the next step, patient's lower limbs were elevated one by one in turn to a height of twelve inches off the couch (12" from heel to couch) and pulse oximeter readings recorded in both the great toes of the patient. After recording the six pulse oximeter readings, measurement of the ankle brachial index was done in all the four limbs.

Ankle brachial index was measured with the help of appropriate standard size sphygmomanometer cuffs and a handheld 8 Mhz vascular Doppler probe. The patients were instructed to remain in the supine position.

As per standard recommendations [27], examination was commenced first in the right arm, followed by the right leg, left leg and finally in the left arm. This was done because blood pressures may vary during the time of examination and the blood pressures at the two arms in the beginning and the end of the examination would provide some quality control.

Measuring of the brachial pressure was done by placing the blood pressure cuff on the arm, with the arm at the left of the heart. The brachial pulse of the patient was palpated and the transducer of the probe was positioned over it after placing the ultrasound gel on the antecubital fossa. This was done to maximize the intensity of the signal. Cuff was inflated about 20 mm Hg over and above the expected systolic pressure. On disappearance of the Doppler signal, the cuff was slowly deflated at a rate of 1 mm Hg per second. The pressure at the time of re-appearance of the Doppler signal was taken as the brachial systolic pressure.

Measurement of the ankle pressure was done by placing the appropriately sized blood pressure cuff immediately above the malleoli. Ultrasound gel was applied to the skin over the dorsalis pedis artery pulse and the posterior tibial artery pulse.



The dorsalis pedis pulse is usually readily palpable slightly lateral to the extensor hallucis longus tendon. The dorsal most prominence of the navicular bone also serves as a reliable landmark for palpation [28]. The posterior tibial artery pulse is readily palpable over the Pimenta's Point. The Pimenta's Point is an anatomical landmark for easy location of the posterior tibial artery pulse. It is an imaginary line drawn between the medial malleolus bony prominence and the Achilles tendon insertion. The pulse of the posterior tibial artery will be felt at the exact midpoint of this line when placing three fingers parallel to the leg.

The Doppler probe was moved until the strongest signal was heard and the cuff was inflated first and then slowly deflated as mentioned above for the arms. The pressures for both dorsalis pedis artery and posterior tibial artery were noted. The higher pressure of the two arteries at the ankle was taken as the Ankle pressure for a given leg. The Ankle Brachial Index value was calculated for each leg by taking the higher pressure of the two arteries at the ankle and was divided by the brachial artery systolic pressure. The value was recorded to two decimal places.

Example:

$$\text{Right ABI} = \frac{\text{Highest Pressure in Right Foot}}{\text{Highest Pressure in Both Arms}}$$

After recording of the pulse oximeter and Ankle brachial index values, the patient was instructed to go to the Ultrasound clinic for Duplex ultrasonography of both lower limb arteries within one week of this initial assessment as per their convenience. They were requested to report back with their results after the Duplex scan. In-patients were sent for both lower limb arterial Doppler during their hospital stay prior to discharge.

Duplex ultrasonography was done and peak systolic velocities of eight arteries in each leg were recorded during the examination by the radiologist. The arteries included were:

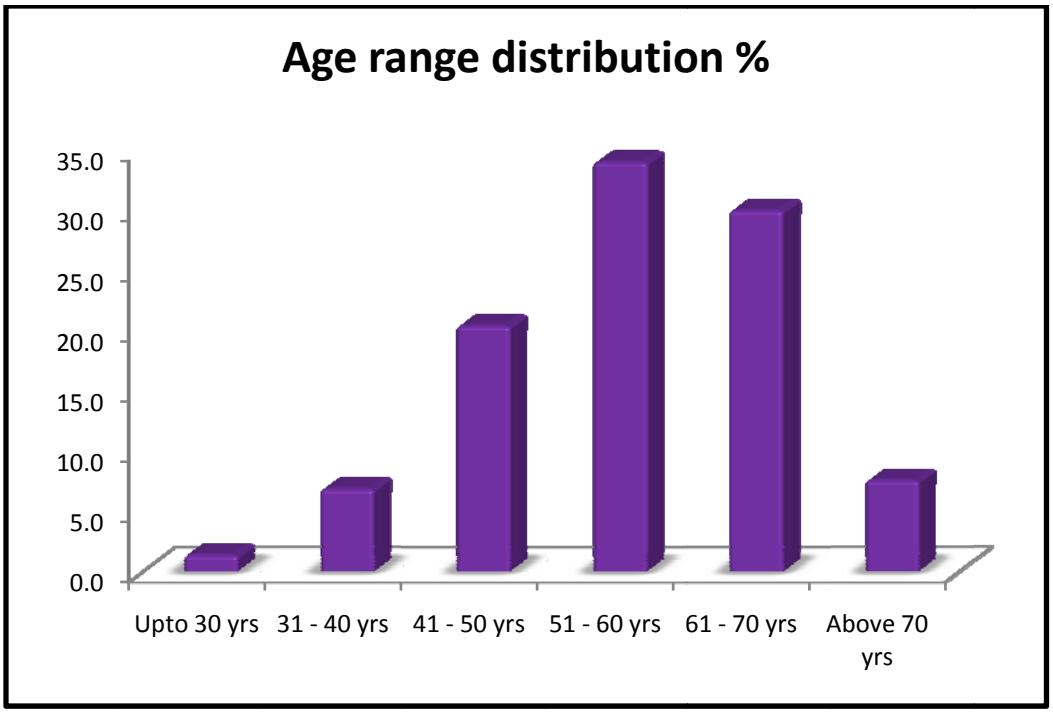
- common femoral artery,
- profunda femoris artery,
- superficial femoral artery,
- popliteal artery,
- peroneal artery,
- anterior tibial artery,
- posterior tibial artery and
- dorsalis pedis artery

The attending radiologist attending to the scan was not aware of the pulse oximeter readings or the Ankle brachial index values of the patient.

The collected data was periodically entered into the master chart and at the end of the study, the data was analysed.

OBSERVATION AND RESULTS

A total of 147 patients were included in the study (as opposed to a calculated sample size of 150). The age distribution of the population is shown below:



The higher age distribution of the sample size may be due to the fact that the sample size also included in-patients. It is more likely for older individuals to require hospitalisation due to diabetes related reasons than younger persons.

The most common diagnoses for which these patients were admitted and met the inclusion criteria are listed below:

- Complicated urinary tract infections
- Chronic kidney disease related complications
- Diabetic ketosis

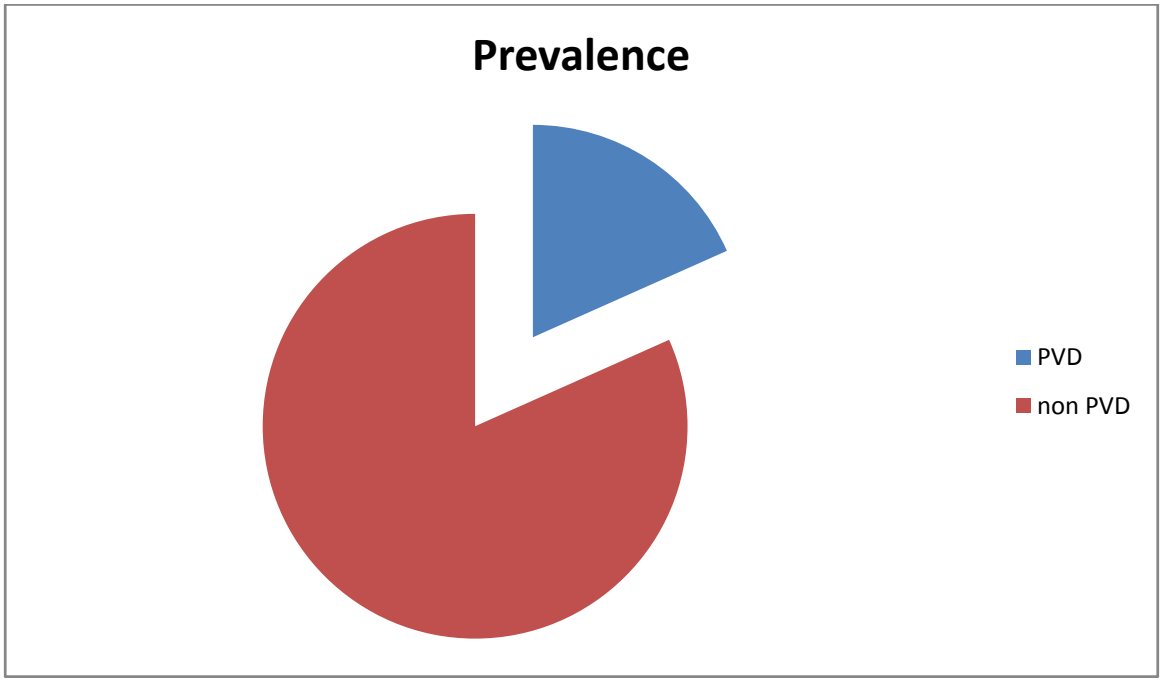
- Community acquired pneumonias
- Diabetic keto acidosis

The vast majority of patients who were admitted in our hospital with diabetes related complications included skin and soft tissue infections such as:

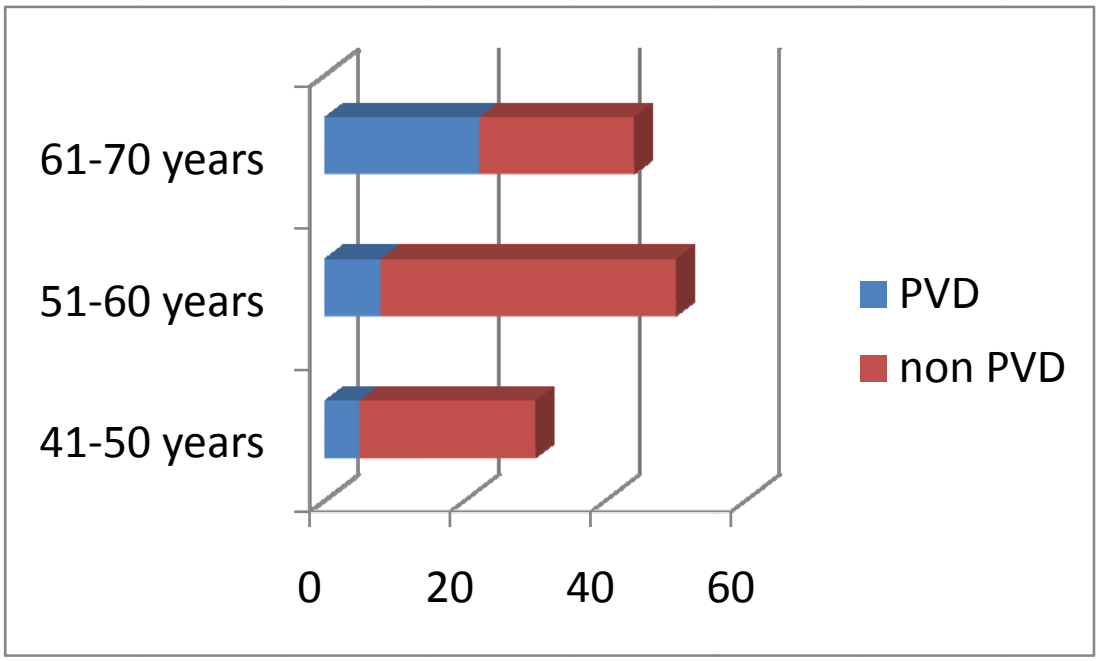
- Cellulitis
- Fasciitis
- Diabetic foot ulcer
- Charcot's neuropathies

These patients were excluded from the study since they did not meet the inclusion criteria.

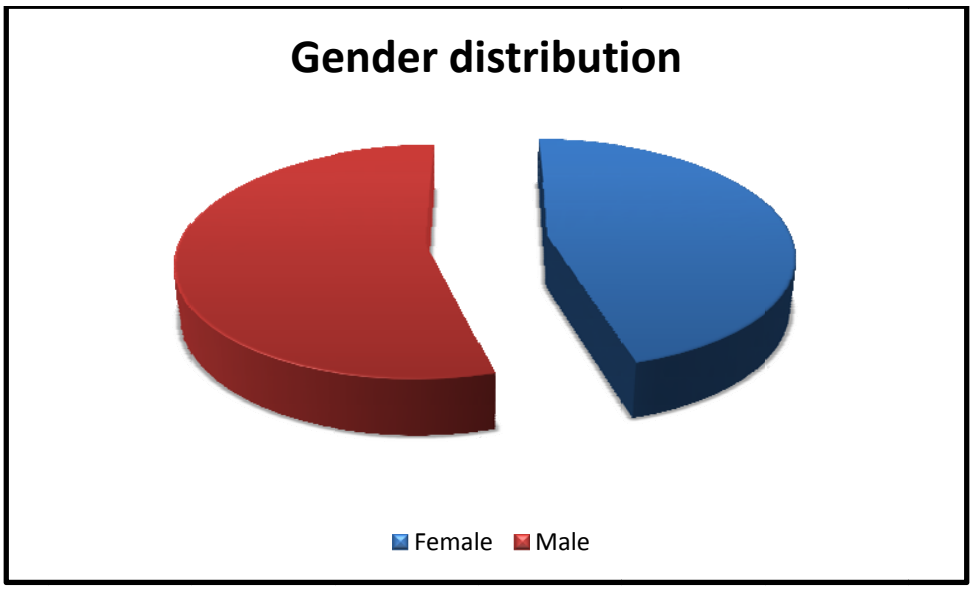
The prevalence of Peripheral vascular disease in the study population was found to be 22.4 %.



It was found on comparing the demographic baseline parameters that the Peripheral Vascular Disease group had a higher percentage of elderly population as depicted in the graph below:

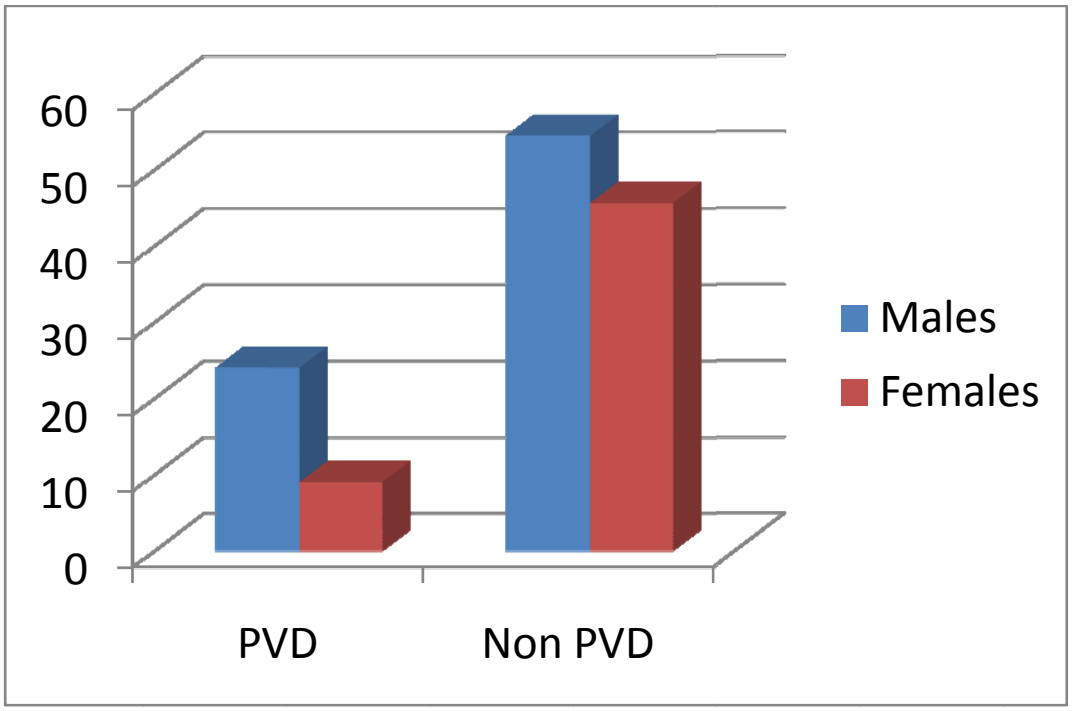


The sex distribution of the study population is as shown:

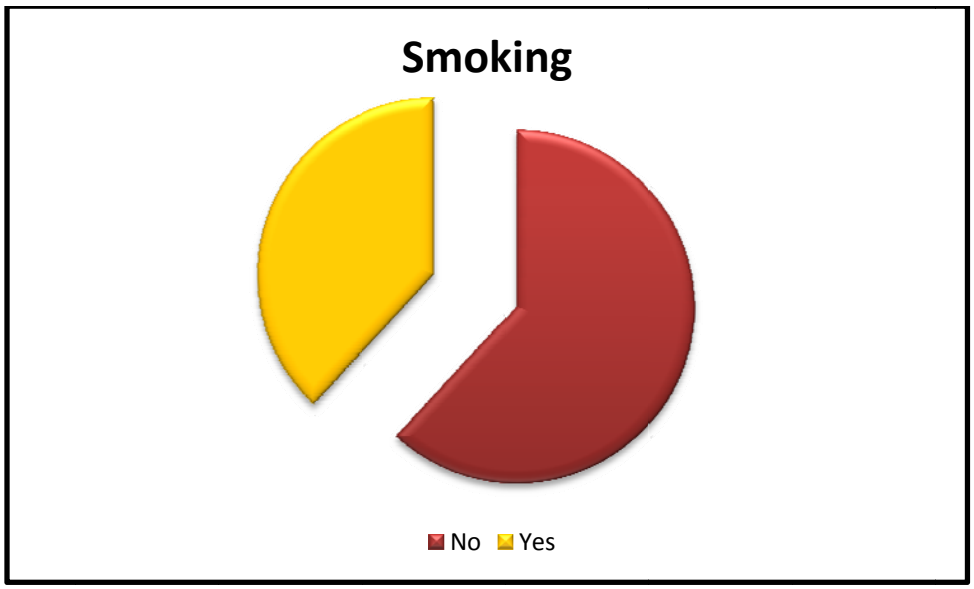


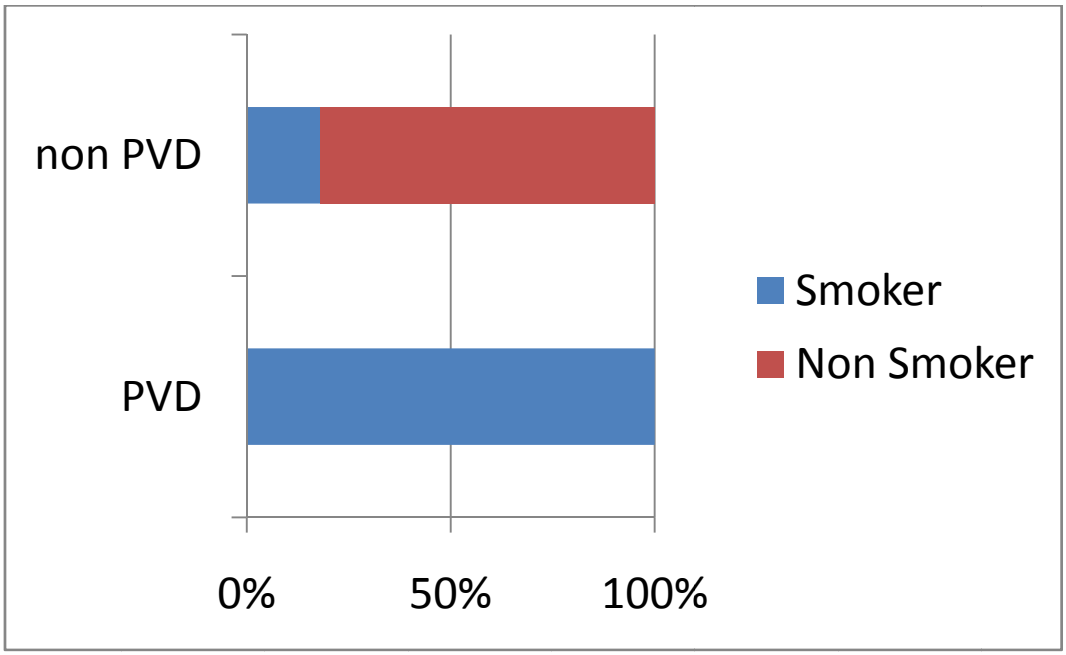
The study population included 45.6 % females and 54.4 % males.

Consistent with previous studies, in our study also, the Peripheral Arterial Disease group had a very significant proportion of males, leading us to believe the conventional teaching that peripheral arterial disease is commoner in the male gender.



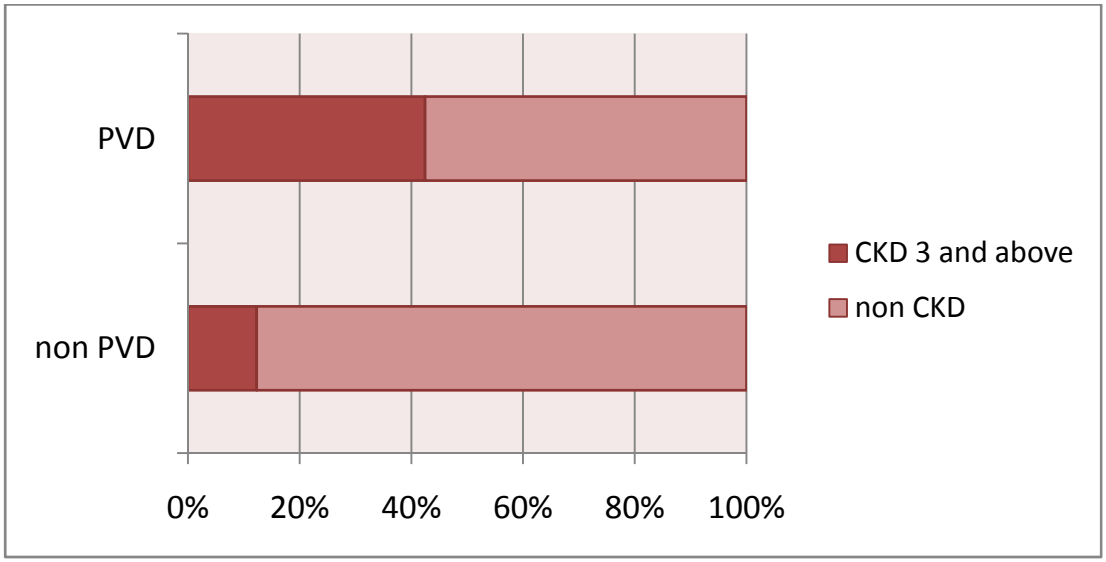
Though the statistical significance of the fact was not tested, all 24 males who were diagnosed to have peripheral arterial disease by Duplex scan in our study turned out to be chronic smokers, with 20 of them continuing to smoke some form of tobacco (cigarettes, beedi et cetera)


Smoking
No
Yes


non PVD
PVD
0%
50%
100%
Smoker
Non Smoker

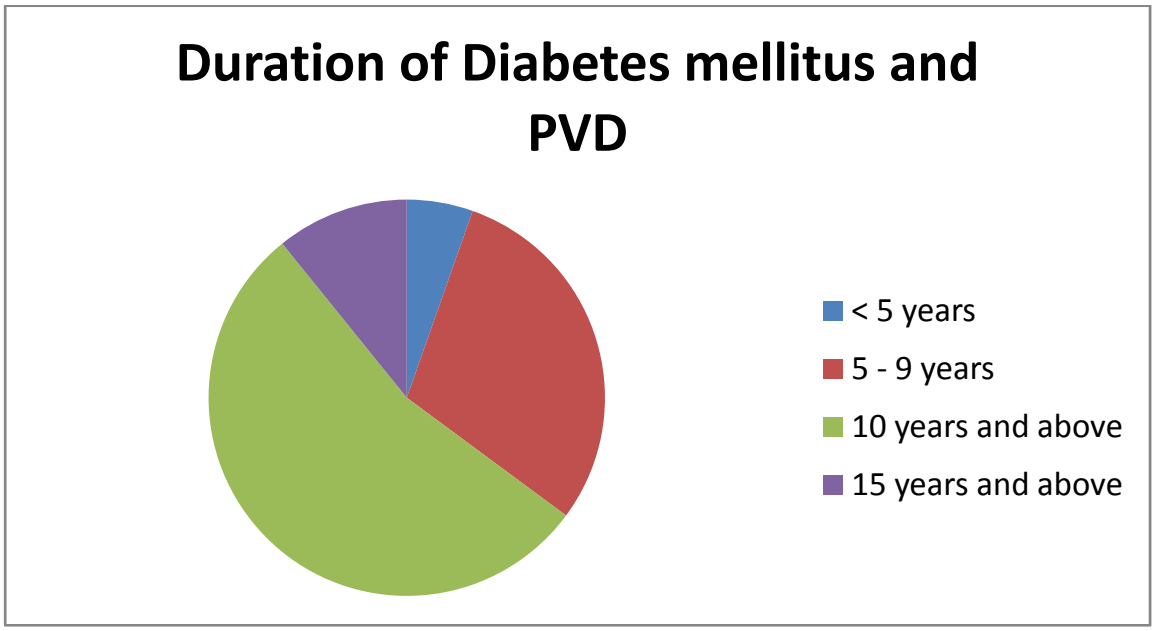
It was observed in our study population, while analysing the association of peripheral arterial disease with other micro vascular or macro vascular complications of diabetes mellitus, that a majority of the study population diagnosed to have peripheral arterial disease also had diabetic nephropathy with an estimated glomerular filtration rate below 60 ml per minute qualifying as Chronic Kidney Disease Stage 3 and beyond.

It was observed that 14 out of 33 patients diagnosed by Duplex to have Peripheral arterial disease also had diabetic nephropathy. In contrast, only 14 out of the remainder of 114 patients had chronic kidney disease in the non PVD group.



The duration of the diabetes mellitus and its relation to the prevalence of peripheral arterial disease was also studied by perusing the baseline demographic parameters. While previous studies have reported almost twice as much frequency of peripheral arterial disease in long standing diabetes mellitus, considered as greater than 10 years of disease, our study population had a mixed distribution.

Out of the 33 patients diagnosed to have peripheral arterial disease, roughly equal number of patients fell into either category of 5-10 years and 10 years and above.



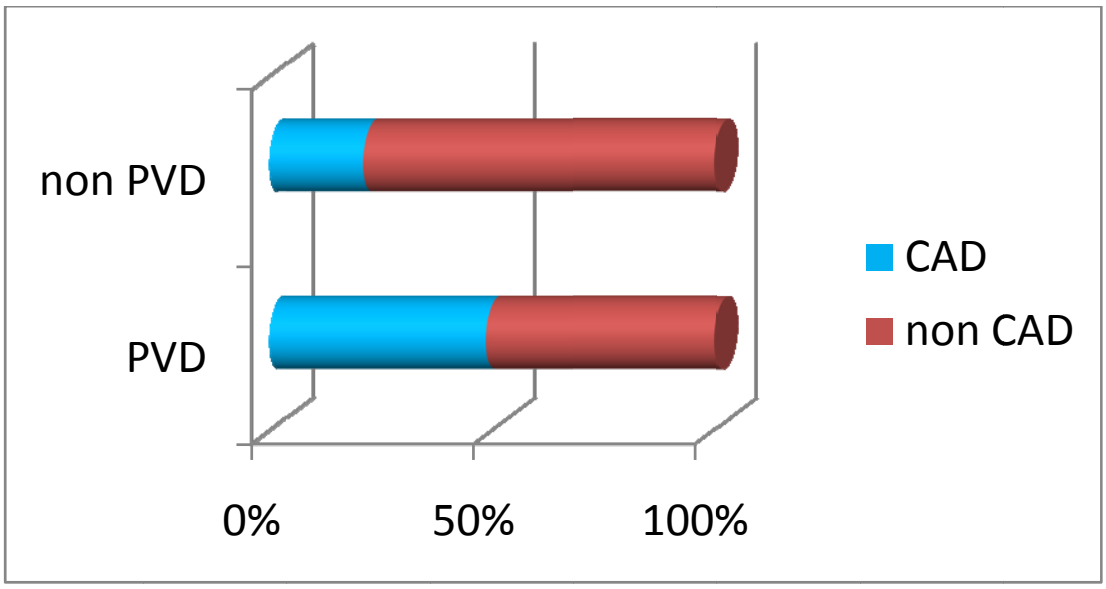
Ankle brachial Index has always been also studied as an independent predictor of cardio vascular events in relation to coronary artery disease related events. Though results from past studies have been mixed, the overall consensus is that a low ankle brachial index does confer greater risk of patient succumbing to coronary artery disease rather than the peripheral artery disease itself.

In our study population too, a majority of the patients in the Peripheral Vascular Disease group had evidence of coronary artery disease in the form of:

- Angiogram proven coronary artery disease
- Previous myocardial infarctions
- Ischemic cardiomyopathy

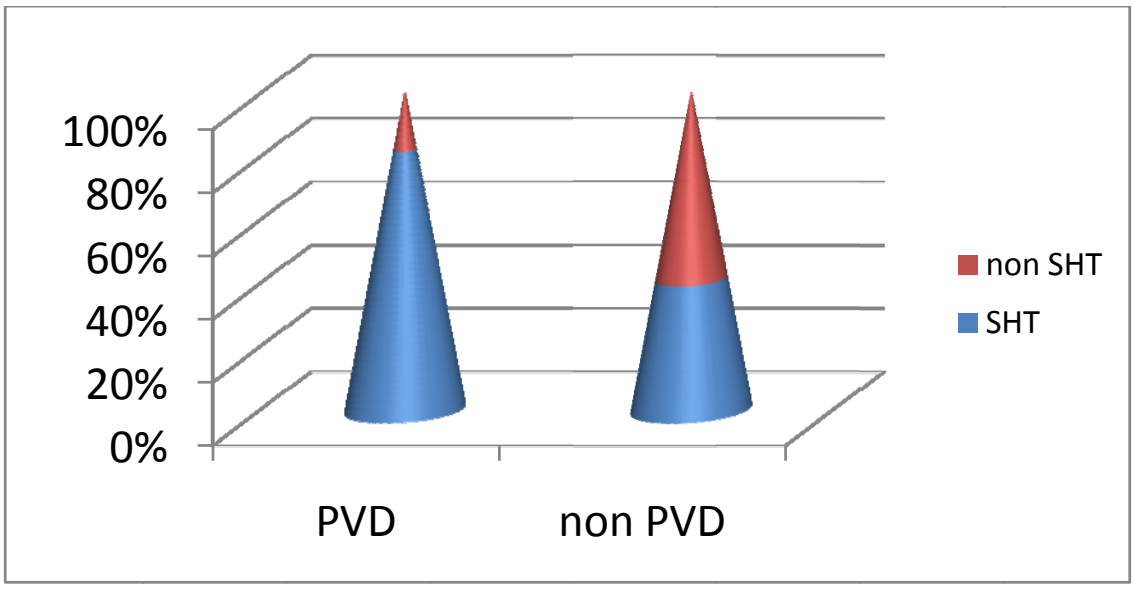
While 16 out of the 33 patients diagnosed to have peripheral arterial disease also had proven coronary artery disease, a mere thirty patients out of the remainder only had ischemic heart disease.

This is consistent with the available evidence that peripheral artery disease and coronary artery disease share similar pathogenetic mechanisms and hence either one heralds the other or both may co-exist.



Most of the studies have associated the presence of peripheral arterial disease in diabetes mellitus and the coexistence of systemic hypertension. In line with this well known fact, our study population also exhibited similar trends.

27 out of the 33 patients diagnosed to have peripheral arterial disease were also found to have co-existent systemic hypertension. In the non PVD group, 42 out of the remaining 114 patients had systemic hypertension.

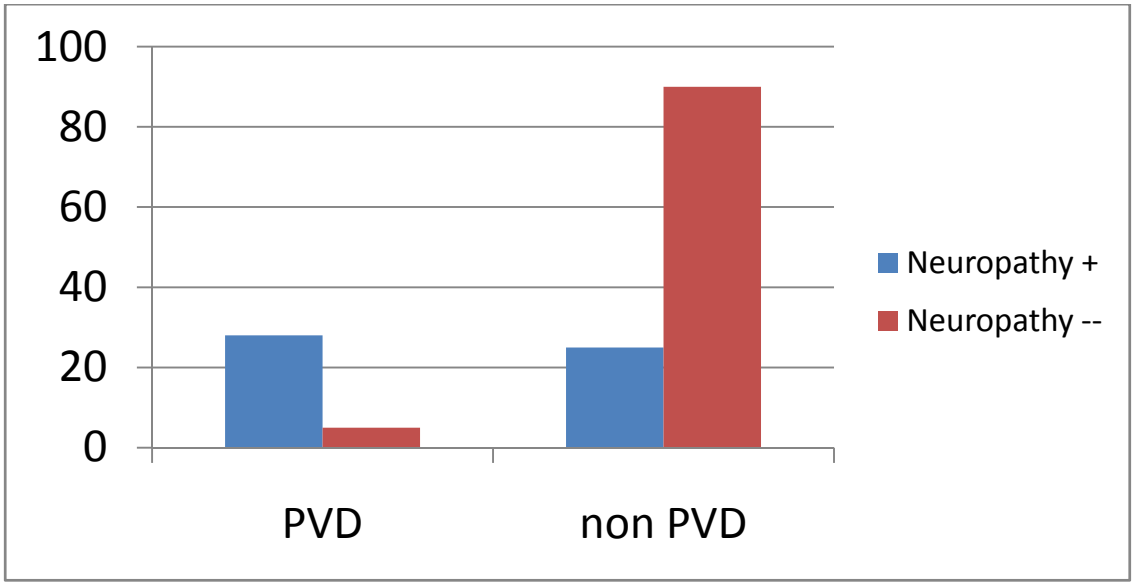


The other micro vascular complication that was compared for its frequency of occurrence in patients with the macro vascular complication of peripheral arterial disease was diabetic neuropathy.

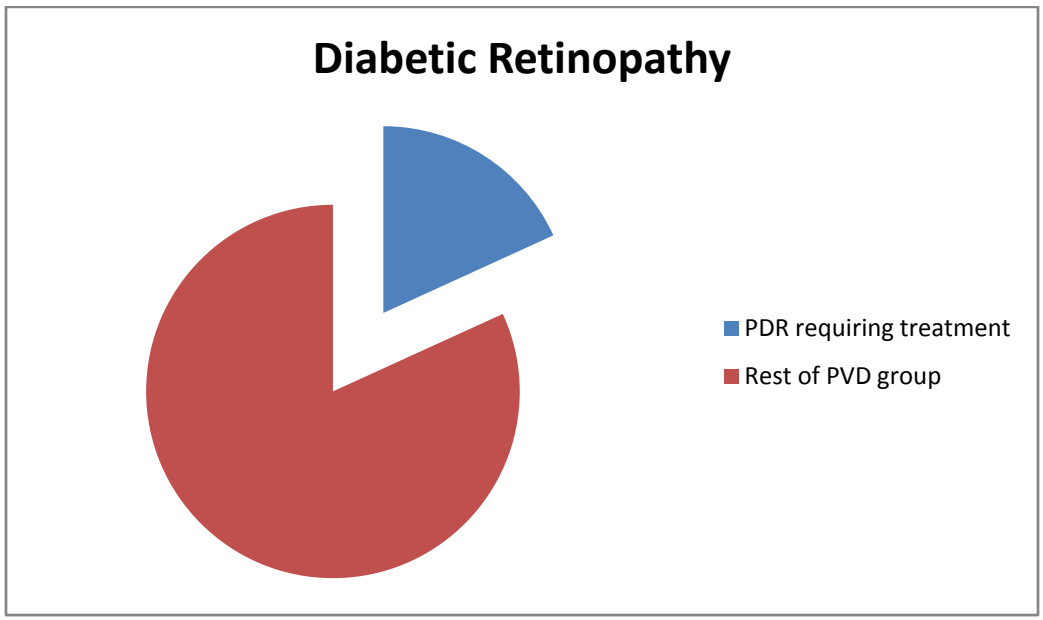
The most common form of neuropathy that occurs in diabetes mellitus, especially long standing diabetes mellitus with poor glycemic control, is Distal Sensory Peripheral Neuropathy. It usually occurs in a glove and stocking distribution.

The co-existence of peripheral arterial disease and peripheral neuropathy heightens the risk of development of diabetic foot ulcers and eventually the diabetic foot syndrome which necessitates lower extremity major amputation at some point in time.

In our study population, 28 out of 33 patients had evidence of diabetic peripheral neuropathy, either by biothesiometry or by monofilament testing.



In our study population, 6 patients in the Peripheral Vascular Disease group had Proliferative Diabetic Retinopathy for which they had undergone laser photocoagulation treatment. However the other patients were not screened for the presence or absence of Diabetic Retinopathy and hence even its chance association with Peripheral arterial disease cannot be commented upon.

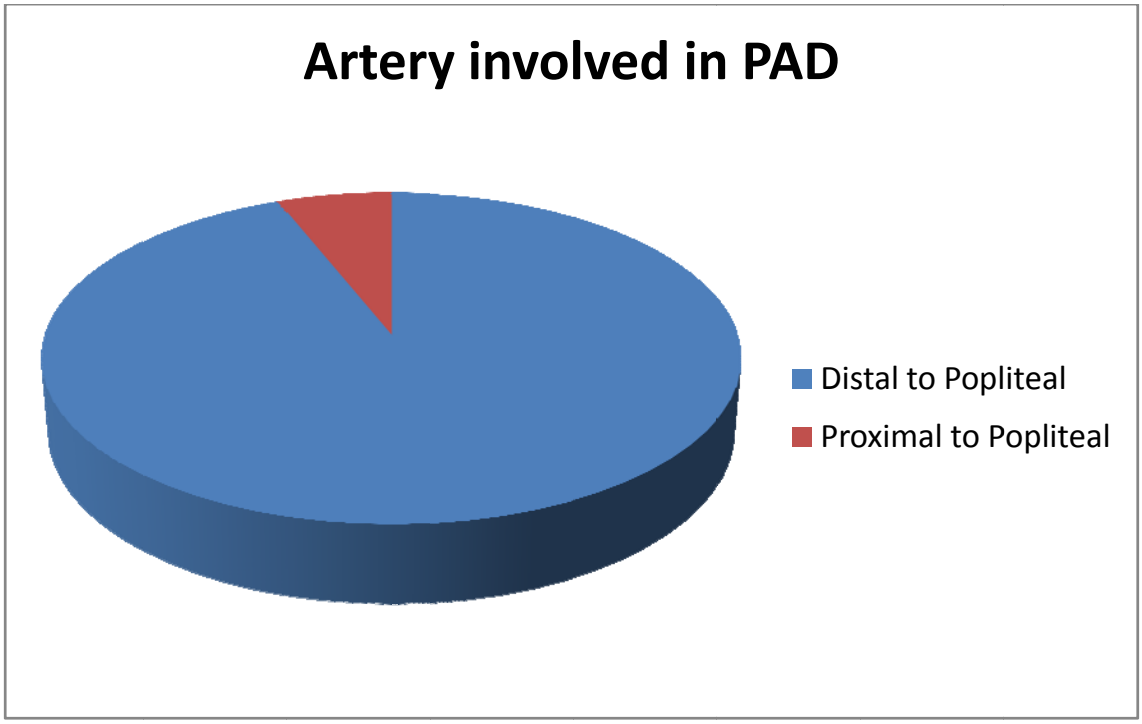


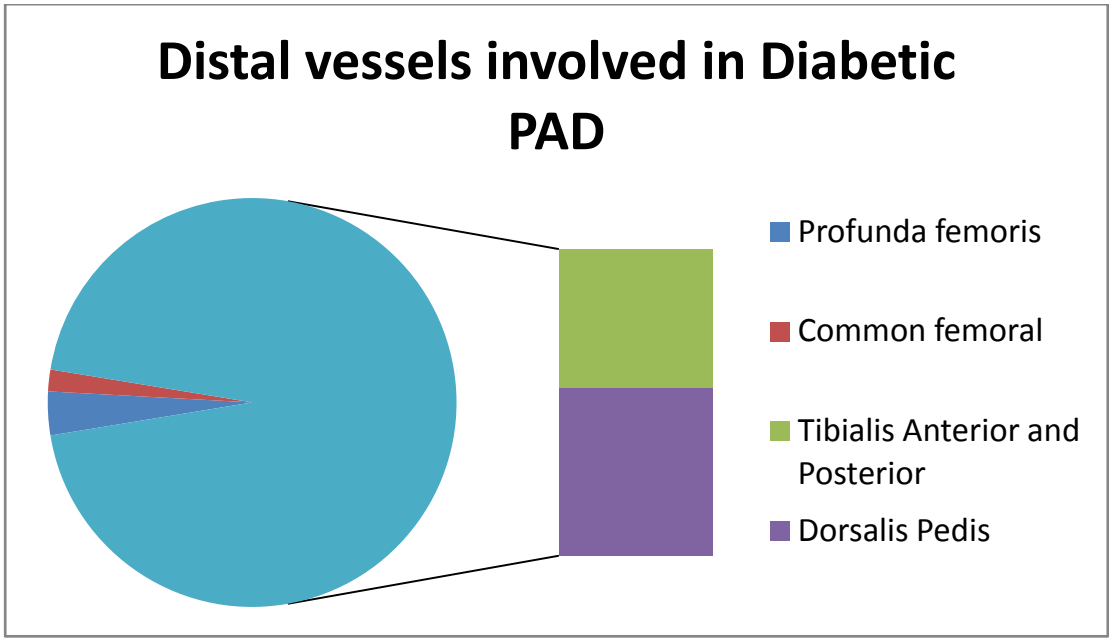
As discussed in the introduction and review of literature sections, peripheral arterial disease in diabetes mellitus is multi-segmental and distal in its involvement.

Validating this view, the Duplex results of our study population also revealed involvement of predominantly distal vasculature. Only 2 patients had monophasic flow in the common femoral artery and profunda femoris arteries. The rest of the patients had involvement distal to the popliteal artery.

A majority of the patients had patchy involvements with multiple segments affected. This was recorded as monophasic flow in the area of multiple arteries in the same patient.

The most common artery involved was the dorsalis pedis artery.





Most of the patients who had monophasic flow recorded in the dorsalis pedis artery also had involvement of the posterior tibial artery. A set of patients also had additional involvement of the anterior tibial artery.

Since the peroneal artery is more posterior in location and supplies comparatively lesser area in the lateral aspect of the lower extremity, our radiologist attendees do not screen the peroneal artery for flow abnormalities.

The collected data were analysed with IBM.SPSS statistics software 23.0 Version.

To describe about the data descriptive statistics, frequency analysis, percentage analysis were used for categorical variables and the mean & S.D were used for continuous variables.

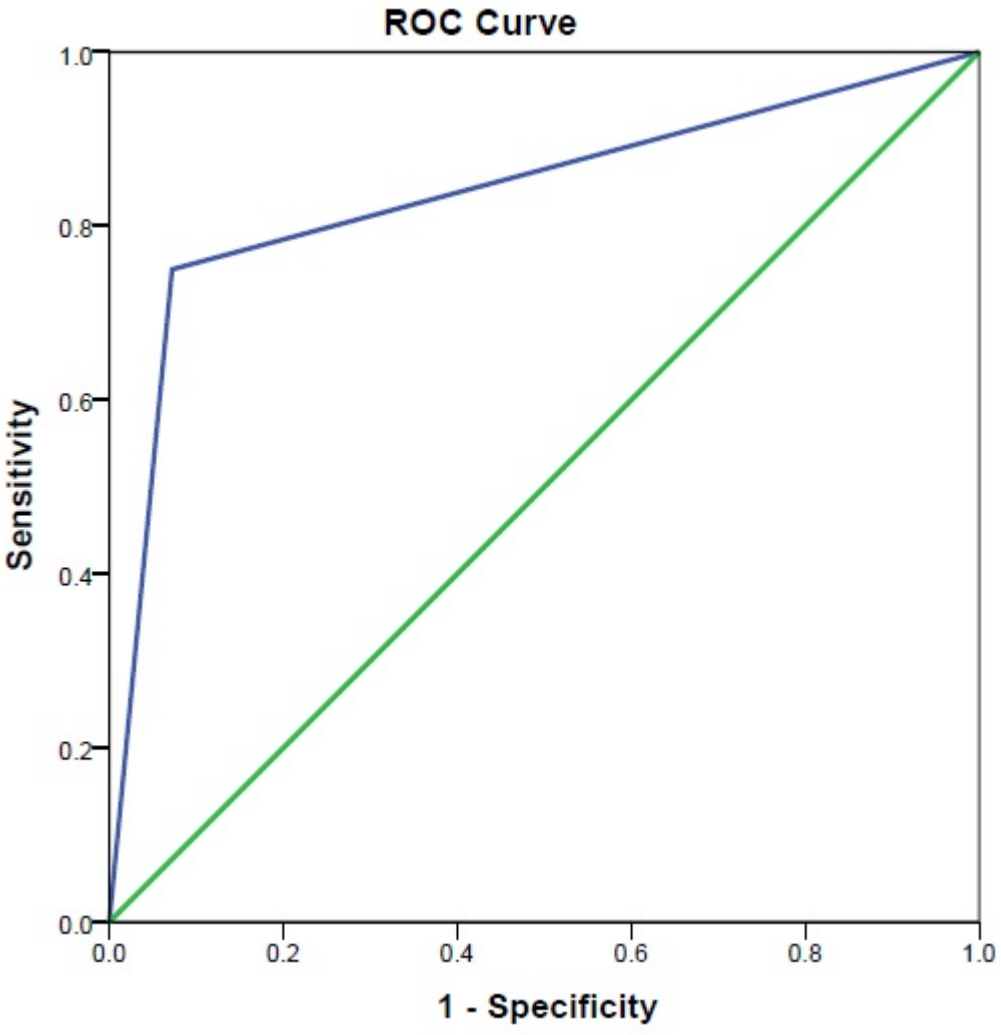
To find the Accuracy, Sensitivity, Specificity, Positive Predictive Value and Negative Predictive Value the appropriate formulae was used with Received Operating Curve (ROC). In the above statistical tool the probability value .05 is considered as significant level.

Net sensitivity = [sensitivity of test 1 + sensitivity of test 2 – (sensitivity of test 1 × sensitivity of test 2)] and Net specificity = [specificity of test 1 x specificity of test 2]

SENSITIVITY, SPECIFICITY, PPV, NPV OF PULSE OXIMETRY

Count

		Pulse Ox		
		Present	Absent	Total
Duplex	Abnormal	27	9	36
	Normal	8	103	111
Total		35	112	147



SENSITIVITY, SPECIFICITY, PPV, NPV OF PULSE OXIMETRY

	PULSE OXIMETRY
SENSITIVITY % (95% CI)	77.14 %
SPECIFICITY % (95% CI)	91.96 %
POSITIVE PREDICTIVE VALUE (95% CI)	75.00 %
NEGATIVE PREDICTIVE VALUE (95% CI)	84.55 %

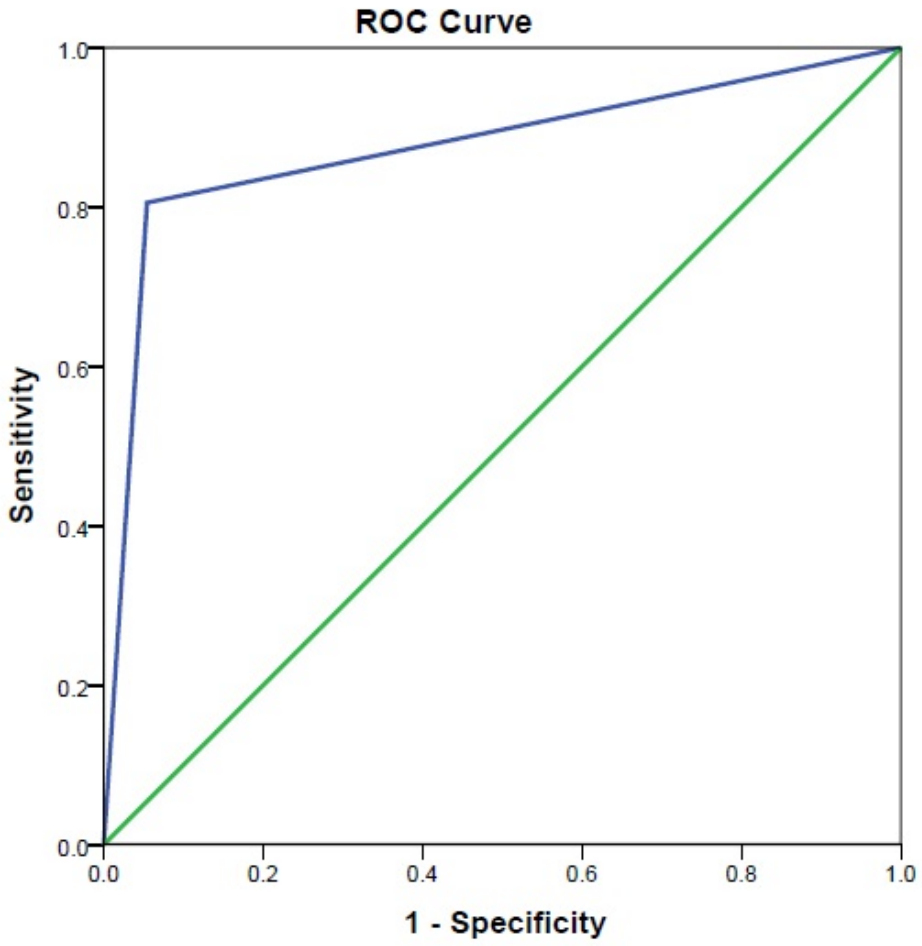
The results in our study are comparable to the previous study done in 2012 in a tertiary care centre in Tamil Nadu which had similar results.

SENSITIVITY, SPECIFICITY, PPV, NPV OF

ANKLE BRACHIAL INDEX

Count

		ABI		
		Present	Absent	Total
Duplex	Abnormal	29	7	36
	Normal	6	105	111
Total		35	112	147



SENSITIVITY, SPECIFICITY, PPV, NPV OF

ANKLE BRACHIAL INDEX

	ANKLE BRACHIAL INDEX
SENSITIVITY % (95% CI)	82.86 %
SPECIFICITY % (95% CI)	93.75 %
POSITIVE PREDICTIVE VALUE (95% CI)	80.56 %
NEGATIVE PREDICTIVE VALUE (95% CI)	94.59 %

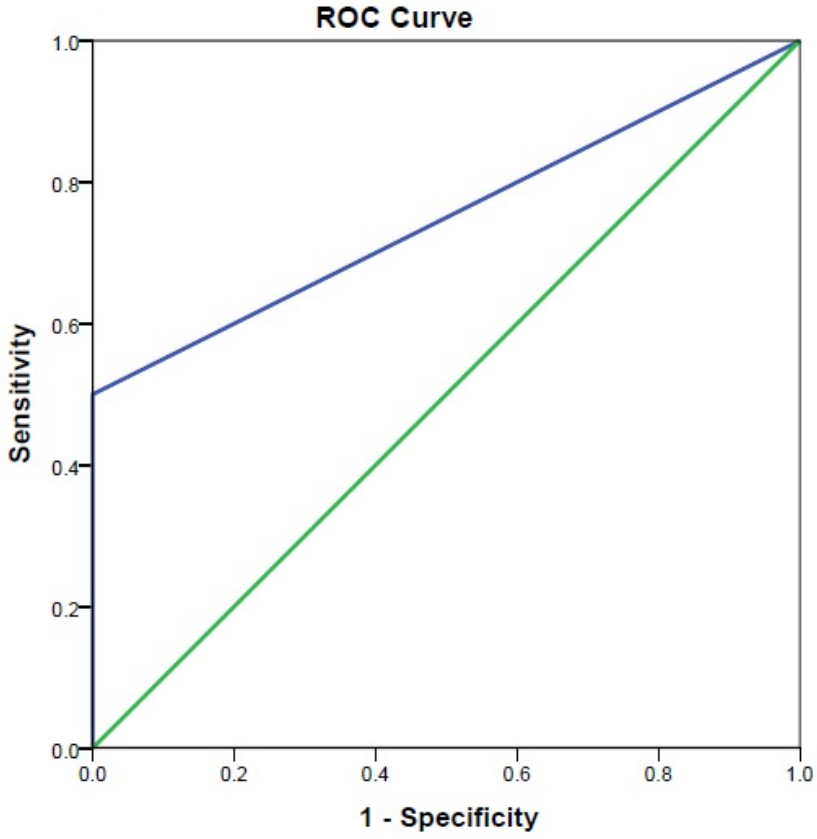
The comparison of these values with previous studies is dealt with in the Discussion session.

SENSITIVITY, SPECIFICITY, PPV, NPV OF

COMBINATION PARALLEL TESTING

Count

		COMBINATION		
		Present	Absent	Total
Duplex	Abnormal	29	3	32
	Normal	2	113	115
Total		31	116	147



SENSITIVITY, SPECIFICITY, PPV, NPV OF

COMBINATION PARALLEL TESTING

	COMBINATION (PARALLEL TESTING)
SENSITIVITY % (95% CI)	93.55 %
SPECIFICITY % (95% CI)	97.41 %
POSITIVE PREDICTIVE VALUE (95% CI)	90.63 %
NEGATIVE PREDICTIVE VALUE (95% CI)	98.26 %

DIAGNOSTIC ACCURACY OF THE TESTS:

TEST	**DIAGNOSTIC ACCURACY**
PULSE OXIMETRY	84.55 %
ANKLE BRACHIAL INDEX	88.30 %
COMBINATION TESTING	95.48 %

DISCUSSION

The prevalence of peripheral arterial disease in our population was fairly high. The landmark Chennai Urban Population Study, done almost two decades ago, reported a much lower prevalence of about 6.3% in diabetics – at that time, it was in stark contrast to the Western literature which had prevalence reports between 21% (United States) to 42% (Greece).

More recent studies however, even in our country, have agreed upon increased prevalence of peripheral arterial disease in our population. All the studies have reported prevalence data upwards of 25%. Even the Chennai Urban Population Study sample population was followed up and it was found that progression of peripheral arterial disease was seen in roughly 20% of the patients.

In tune with above reports even our study population has 22.4 % prevalence of peripheral arterial disease.

In our study population, Peripheral arterial disease was found to be higher in the 61-70 age group (40% of studied sample) followed by the 51-60 age group (26% of the studied sample). In a similar previous study by Satheesh Kumar et al. the maximum percentage of Peripheral artery disease was seen in the 51-60 age group. This could be due to the fact that our sample size had a substantial percentage of older people when compared to that study as we have included in-patients with diabetes mellitus also.

It was also observed that the Male gender and current smokers group had a greater prevalence of Peripheral arterial disease.

Our unit of analyses was patient and not limb as done by other studies [29, 30]. Since the factors that are concerned with Peripheral Vascular Disease are clustered within the individual and because Peripheral Vascular Disease is a generalized process, it was decided that doing patient level analysis was better than doing than extremity level analysis.

We found that for asymptomatic individuals with diabetes mellitus, pulse oximetry performed as efficiently as Ankle brachial index if not better and the combination of both could be used as an effective screening tool. On combination of the two tests, in parallel testing scenario, the accuracy, sensitivity, specificity and predictive values increased.

In terms of external validity, even though the study was performed at a tertiary care centre and the characteristics of the study population may be different from the group of patients attending primary health centres, there are no strong reasons to argue that the results of this study would not be suitable to them. This study would be applicable to all patients with diabetes mellitus who are currently asymptomatic with regard to Peripheral Vascular Disease.

Previous studies which tried to assess the utility of pulse oximetry as a potential screening test for Peripheral Arterial Disease have given mixed results. In a study done in sample of patients suffering from moderate

Peripheral Vascular Disease, sensitivity of pulse oximetry was found to be only 16%.

In another study which was conducted in primary care setting, the sensitivity of pulse oximetry, Ankle Brachial Index and their combination was published to be as 77%, 63% and 86% respectively.10 Specificity was 97% for both tests and 92% for their combination.

Yet another study showing sensitivity and specificity of the modality pulse oximetry to be 87% and 87% respectively concluded that pulse oximetry could be harnessed as an effective, cheap, simple, non invasive screening technique akin to Ankle Brachial Index in assessing Peripheral Vascular Disease.

Previous trials have opined that pulse oximetry was effective not only in detecting asymptomatic cases but also was able to stratify Peripheral vascular disease into different grades of severity. [31]

Although a few studies showed that Ankle Brachial Index performs better only in cases of severe disease, whereas in our study it was found to perform satisfactorily well among patients without symptoms of peripheral vascular disease. In a previous study, subgroup analysis was done to check if these tests performed differently across different parameters, which was not done in our study.

Our study was designed carefully to avoid biases which are commonly encountered diagnostic accuracy studies:

- Spectrum bias
- Diagnostic review bias
- Verification bias
- Misclassification bias

In the first place, we have included only asymptomatic patients with regard to Peripheral Vascular Disease, thereby avoiding spectrum bias. Spectrum bias occurs where test performances are assessed based on severe cases only. Accuracy of these tests has been previously established in severe cases.

This selection criterion of including only asymptomatic patients also tried to reduce to some extent, the bias that occurs when the course of the disease and its severity depending on its duration has an impact on the tests being studied. The tests may have varying performances with regard to disease duration.

The Diagnostic review bias was nullified by blinding the radiologist attendee who performed the Duplex ultrasonography. Hence since the reference standard tests were performed independently of the index tests, we avoided the diagnostic review bias.

Thirdly, by making all patients to undergo all the three tests, the verification bias was avoided. Finally, we were not able to perform Contrast angiography for all the patients. Duplex scan which was used as the reference standard test has very high sensitivity and specificity [32] but it is not perfect since it is not the gold standard. This leads to the possibility of mis-classification bias. However, this misclassification was likely to be non-differential affecting the results only slightly.

There are a few limitations in the study. Firstly, since a single investigator performed both the index tests, namely pulse oximetry and Ankle Brachial Index, the result of one might have influenced that of the other. Secondly, we could not measure test reliability in terms of inter-observer and intra-observer variability. Finally, we could not study the effect of a few covariates like occupation, control of diabetes, extent of physical activity and lipid profile, which have a bearing on development of Peripheral Vascular Disease. Future research could study the effect of these variables with a larger sample size.

CONCLUSION

Pulse oximetry is as good as Ankle Brachial Index in the initial screening of patients with asymptomatic Peripheral Vascular Disease.

It will be an ideal cheap simple-to-use potential screening tool that can be used at the grassroots level by medical and paramedical personnel alike.

The combination of the two tests, that is Pulse oximetry and Ankle Brachial Index has an even higher sensitivity and diagnostic accuracy than either of the two tests alone.

Diabetic patients more frequently develop symptomatic forms of Peripheral Vascular Disease, resulting in majority of major amputation surgeries in the lower extremities.

The odds for major lower extremity amputation in patients with diabetes mellitus are 12 times when compared with that of the non-diabetic population. Early detection and timely intervention can prevent this significant disability.

It has been also been validated that Peripheral Vascular Disease is correlated with cardiovascular events such as Myocardial Infarction and Stroke. The Toe Brachial Index may be an even better tool to predict cardiovascular outcomes.

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ANNEXURES

- **PROFORMA**
- **MASTER CHART**
- **CONSENT FORM**
- **ETHICS COMMITTEE APPROVAL CERTIFICATE**

PROFORMA

Name: Age/sex:

Address: IP NO/OP NO:

Duration of Diabetes:

Complications: CAD / CVD / PVD / DR / CKD / DSPN

Co-morbid illness: (if any)

Smoker: Yes / No

Pulse Oximetry:

• Right Index finger • Left index finger

• Right Great Toe • Left Great Toe

• Right Great Toe at 12 inch elevation

• Left Great Toe at 12 inch elevation

ABI:

• Right • Left

Duplex Ultrasonography : To attend scan at Room 46A, Ground Floor, Dept. Of Radiology, Surgery Block

MASTER CHART

S.No	Age	Sex	dDM	Mic Mac	CMD	SMK	RF	LF	RT	LT	RT“	LT“	RABI	LABI	Duplex
1	35	F	5	-	-	-	98	99	98	98	98	99	1.23	1.25	N
2	76	F	22	CKD CAD	SHT HypoT	-	98	98	95	97	94	96	0.71	0.82	MONOPHASIC FLOW RT. PA, DP
3	44	F	7	DSPN	SHT	-	98	98	99	98	98	98	1.09	1.10	N
4	56	M	10.5	DSPN CAD	SHT	Y	99	98	96	96	96	95	0.76	0.74	N
5	62	M	20	DSPN CAD CKD DR	SHT	N	98	98	96	95	95	96	0.66	0.62	MONOPHASIC FLOW RT. ATA PTA DP LT. PA, ATA, PTA, DP
6	65	M	9	CKD CAD	SHT	N	98	99	97	98	97	98	0.97	0.99	N
7	75	M	30	CKD CAD DR DSPN	SHT HypoT COPD	Y	97	97	97	97	97	97	0.97	0.97	ATHEROMATOUS NARROWING +
8	49	M	5	-	-	-	98	99	98	99	98	98	1.27	1.30	N
9	51	F	10	DSPN	SHT	-	98	98	97	97	97	97	1.05	1.15	N
10	32	F	2	-	-	-	99	99	99	99	99	99	1.22	1.19	N
11	71	F	8	CKD	SHT	-	98	98	97	97	97	97	1.09	1.10	N
12	66	M	10	CAD	SHT	Y	99	99	99	99	99	99	1.22	1.26	N
13	78	M	12	CAD	SHT	Y	98	98	97	97	97	97	0.98	.97	ATHEROMATOUS
				CKD DR											NARROWING +
14	48	F	6	-	SHT	-	98	98	99	99	98	98	1.18	1.00	N
15	63	F	11	DSPN CAD	SHT	-	99	99	98	98	98	98	1.07	1.11	N
16	38	M	6	-	SHT	Y	97	98	98	98	97	97	1.11	0.98	N
17	58	M	15	DSPN CAD	SHT	Y	99	98	97	97	96	97	0.70	0.79	MONOPHASIC FLOW RT. DP LT. PTA, DP
18	88	M	18	CKD CAD	SHT	-	97	97	97	97	95	95	0.81	0.82	ATHEROMATOUS NARROWING
19	54	M	4	CAD	SHT	Y	98	98	98	98	98	98	1.1	0.97	N
20	70	M	14	DR CAD CKD	SHT	Y	98	97	98	97	97	96	0.92	0.94	N
21	65	F	6	DSPN	-	-	97	97	97	97	97	97	0.99	0.98	MONOPHASIC FLOW RT. PTA, ATA
22	54	F	2	-	-	-	99	99	99	99	99	99	1.09	1.10	N
23	61	M	6	DSPN CAD	-	Y	98	98	97	97	96	96	0.95	0.97	N
24	45	M	5	-	-	-	99	99	99	99	99	99	1.10	1.18	N
25	67	M	17	CAD CKD DSPN	SHT	-	98	98	96	96	95	95	0.75	0.80	MONOPHASIC FLOW RT. PA, ATA, PTA, DP
26	55	M	3	CAD	SHT	Y	98	98	98	97	97	97	0.95	0.95	N
27	60	M	4	-	SHT	Y	99	99	99	99	99	99	0.92	0.99	N

28	70	F	9	DSPN CKD	SHT	-	99	97	98	95	96	95	0.80	0.69	MONOPHASIC FLOW LT. DFA, PA, ATA, PTA, DP
29	56	M	10	DSPN	SHT	Y	98	99	95	97	95	96	0.70	0.90	MONOPHASIC FLOW RT. PA, ATA,
30	51	F	5	-	-	-	99	99	99	99	98	99	1.10	0.96	N
31	60	M	10	CAD	SHT	Y	98	98	98	98	97	98	1.00	1.17	N
32	48	F	2	DSPN	-	-	98	98	98	98	96	95	0.89	0.79	MONOPHASIC FLOW LT. PTA DP
33	61	M	7	-	-	-	98	98	98	98	97	98	1.05	1.14	N
34	78	F	10	DSPN CAD	SHT	-	97	97	97	97	97	97	0.94	0.95	ATHEROMATOUS NARROWING +
35	56	F	7	-	-	-	99	99	99	99	99	98	1.02	1.22	N
36	36	M	3	-	-	Y	99	99	99	99	99	99	1.30	1.23	N
37	68	M	8	CAD	SHT	Y	98	98	97	98	97	97	0.92	0.95	ATHEROMATOUS NARROWING +
38	54	F	5	-	-	-	98	98	98	98	98	98	1.05	1.15	N
39	48	M	4	-	-	Y	99	99	98	98	98	98	1.11	1.24	N
40	55	M	8	-	SHT	-	98	98	98	98	98	98	1.03	1.08	N
41	64	F	16	DSPN DR CAD	SHT	-	98	99	96	96	96	95	0.79	0.73	MONOPHASIC FLOW LT. PTA DPA RT. ATA PTA
42	60	M	8	-	-	Y	99	99	99	99	99	99	1.10	0.99	N
43	50	F	5	DSPN	-	-	98	98	98	98	98	99	1.00	0.99	N

44	61	F	6	-	SHT	-	99	98	97	97	96	96	0.79	0.92	MONOPHASIC FLOW RT. PA
45	55	M	5	-	-	-	99	99	99	99	98	98	1.01	1.19	N
46	60	M	4	-	SHT	Y	98	98	98	98	98	98	1.11	1.21	N
47	78	F	11	CKD CAD DR	SHT	-	99	97	98	97	96	96	1.03	0.89	ATHEROMATOUS NARROWING +
48	43	F	5	-	-	-	99	99	98	98	98	98	1.30	1.16	N
49	57	F	7	-	-	-	98	98	98	98	98	97	1.02	1.27	N
50	66	M	8	CAD	SHT	Y	98	98	96	96	96	95	0.75	0.74	MONOPHASIC FLOW LT. DPA RT. PTA, DPA
51	64	M	9	CAD	SHT	Y	99	99	97	97	97	97	0.90	0.89	N
52	59	M	3	-	-	-	97	97	98	98	98	98	1.11	1.20	N
53	60	F	7	-	-	-	98	98	98	98	99	97	1.00	0.95	N
54	55	M	8	DSPN	SHT	Y	98	98	97	97	97	97	1.11	1.26	N
55	51	F	7	-	-	-	99	99	99	99	99	99	1.21	1.31	N
56	66	M	17	DSPN CKD	SHT	Y	97	97	98	94	97	93	0.85	0.68	MONOPHASIC FLOW LT. DFA, PTA
57	69	F	10	DSPN	SHT	-	99	99	96	98	95	95	0.76	0.79	MONOPHASIC FLOW LT. PA, DPA
58	70	F	9	DSPN	SHT	-	98	98	96	98	95	97	0.85	0.95	ATHEROMATOUS NARROWING +
59	46	F	8	-	-	-	99	99	99	99	99	99	1.16	1.20	N
60	39	F	2	-	SHT	-	98	98	98	98	98	98	1.19	1.29	N

61	48	M	6	CAD	SHT	Y	99	99	97	96	97	95	0.82	0.72	MONOPHASIC FLOW LT. ATA, PTA, DPA
62	50	M	1	CAD	SHT	Y	99	99	98	98	98	98	1.20	0.99	N
63	52	F	2	-	-	-	98	98	97	97	97	97	1.14	1.04	N
64	60	M	11	DSPN DR	SHT	Y	99	98	96	96	96	96	0.69	0.75	MONOPHASIC FLOW RT. PTA, ATA, DPA LT. DPA
65	65	F	10	DSPN CKD	SHT	-	97	97	97	98	98	98	0.92	0.96	ATHEROMATOUS NARROWING +
66	40	M	3	-	SHT	-	98	98	98	98	98	97	1.28	1.33	N
67	45	M	6	-	-	Y	99	99	96	96	96	96	0.99	1.09	N
68	72	M	12	CKD DR	SHT	-	98	98	97	97	97	97	0.93	0.90	ATHEROMATOUS NARROWING +
69	64	F	5	DSPN	SHT	-	97	97	97	97	97	98	1.01	0.96	N
70	53	M	5	-	-	Y	98	98	98	98	98	98	1.34	1.44	N
71	52	M	6	-	-	-	99	99	99	99	99	99	1.40	1.20	N
72	56	M	5	-	SHT	Y	98	98	98	98	98	98	1.16	1.18	N
73	47	F	2	-	-	-	98	98	98	98	98	98	1.12	1.10	N
74	58	M	4	-	COPD	Y	98	98	96	96	94	94	0.73	0.72	MONOPHASIC FLOW LT. DPA RT. PA, ATA, PTA
75	75	F	15	DSPN DR CKD	SHT	-	97	97	95	95	95	95	0.79	0.82	MONOPHASIC FLOW RT. PTA
76	45	M	3	-	-	-	99	99	99	99	99	99	0.99	1.19	N

77	39	M	2	-	-	Y	99	99	99	99	99	99	1.12	1.20	N
78	40	F	1	-	-	-	98	98	98	98	98	98	1.18	1.20	N
79	67	F	14	CKD	SHT HypoT	-	98	98	96	96	96	95	0.91	0.78	MONOPHASIC FLOW LT. PTA, DPA
80	68	M	9	CAD	SHT	Y	99	99	96	98	96	98	0.72	0.85	MONOPHASIC FLOW RT. DFA, DPA
81	59	F	5	DSPN	-	-	98	98	98	98	98	97	1.18	1.21	N
82	55	M	2	CAD	SHT	-	99	98	97	97	94	96	0.70	0.86	MONOPHASIC FLOW RT. PTA, DPA
83	44	F	1	-	-	-	98	98	98	98	98	98	1.11	1.09	N
84	50	M	2	-	SHT	Y	99	99	99	99	99	99	1.08	0.91	MONOPHASIC FLOW LT. PTA
85	69	M	17	DSPN CAD CKD	SHT	Y	98	98	96	96	95	94	0.75	0.80	MONOPHASIC FLOW RT. PTA LT. DFA, DPA
86	60	F	10	DSPN	SHT	-	98	98	98	97	97	97	0.94	0.90	N
87	55	M	5	-	SHT	-	99	99	98	98	98	98	1.31	1.30	N
88	62	F	6	DSPN CKD	SHT HypoT	-	99	98	98	98	98	97	0.91	0.99	N
89	48	F	4	-	-	-	99	98	98	98	99	99	1.23	1.27	N
90	52	M	8	-	-	Y	98	98	98	98	98	98	0.92	0.89	N
91	29	M	1	-	-	-	99	99	99	99	99	99	1.38	1.20	N
92	78	F	16	DSPN CAD CKD	SHT	-	98	98	97	97	96	96	0.82	0.80	ATHEROMATOUS NARROWING +

93	65	M	9	-	-	Y	98	98	98	98	98	98	1.09	1.22	N
94	40	F	1	-	-	-	99	99	99	99	99	98	1.21	1.27	N
95	54	M	8	DSPN	SHT	Y	99	99	96	97	96	96	0.76	0.84	MONOPHASIC FLOW RT. DPA
96	50	F	2	-	-	-	99	99	99	99	99	98	1.09	1.17	N
98	60	F	10	DSPN CAD	SHT	Y	99	98	96	97	95	95	0.75	0.80	MONOPHASIC FLOW RT. PTA LT. DPA
99	61	F	5	-	HypoT	-	98	98	98	98	98	98	0.91	1.02	N
100	62	M	10	CKD CAD	SHT	Y	96	99	93	97	93	96	0.64	1.00	MONOPHASIC FLOW RT. CFA, DFA, PTA, DPA
101	54	M	3	-	SHT	-	98	98	98	98	98	98	1.15	1.19	N
102	50	F	6	-	-	-	98	98	97	97	97	97	1.12	1.16	N
103	57	F	4	-	-	-	98	98	98	98	98	98	0.99	1.20	N
104	47	M	10	DSPN	SHT	Y	99	97	97	96	96	94	0.78	0.77	MONOPHASIC FLOW LT. PTA, DPA
105	61	F	7	DSPN	-	-	98	98	95	95	95	95	1.00	0.98	N
106	71	M	20	CKD CAD	SHT	Y	97	97	97	97	97	97	0.92	0.89	ATHEROMATOUS NARROWING +
107	62	F	15	CKD	SHT	Y	98	98	97	97	97	97	1.00	0.98	ATHEROMATOUS NARROWING +
108	40	F	2	-	-	-	99	99	99	99	99	99	1.15	1.25	N
109	46	M	4	CAD	-	Y	98	98	98	98	97	97	0.91	0.90	N
110	70	M	19	CAD	SHT	-	98	97	99	98	97	97	0.92	1.16	N

111	63	M	5	-	SHT	Y	98	99	99	99	99	98	1.24	1.30	N
112	59	F	6	DSPN	HypoT	-	98	98	96	96	95	95	0.99	1.02	N
113	58	F	10	DR	-	-	98	98	98	98	98	98	1.02	1.18	N
114	66	M	8	CKD	SHT	-	97	98	94	98	94	96	0.70	0.86	MONOPHASIC FLOW RT. ATA, PTA, DPA
115	65	F	5	DSPN	-	-	98	98	98	98	97	97	1.03	0.98	N
116	46	M	4	-	SHT	Y	98	98	98	99	98	98	1.22	1.20	N
117	67	M	16	DSPN CAD CKD	SHT	Y	99	99	96	97	95	95	0.75	0.76	MONOPHASIC FLOW RT. DPA LT. PTA, DPA
118	70	F	14	CAD DSPN	HypoT	-	98	99	96	96	96	96	0.68	0.70	MONOPHASIC FLOW LT. PA RT. DPA
119	41	M	1	-	-	-	99	99	99	99	99	99	1.30	1.24	N
120	50	M	2	CAD	SHT	Y	98	98	98	98	98	98	0.99	0.85	MONOPHASIC FLOW LT. DPA
121	53	M	3	CAD	SHT	Y	97	98	97	98	97	97	1.04	1.00	N
122	60	F	8	DSPN DR	-	-	98	98	98	98	98	98	1.00	0.94	N
123	48	F	7	-	-	-	99	99	98	98	98	98	1.20	1.09	N
124	50	M	4	DR	SHT	Y	98	98	97	96	97	94	1.00	0.70	MONOPHASIC FLOW LT. PTA, DPA
125	30	M	2	-	-	-	98	98	98	98	98	98	1.22	1.20	N
126	63	M	5	CAD CKD	SHT	Y	98	98	95	97	95	96	0.80	0.93	MONOPHASIC FLOW LT. PA

127	57	F	8	DSPN	-	-	99	99	99	98	98	98	1.25	1.20	N
128	69	F	18	DSPN CKD CAD	SHT HypoT	-	98	98	96	95	96	94	0.90	0.76	MONOPHASIC FLOW LT. ATA, PTA, DPA
129	63	M	10	CAD	SHT	Y	99	98	98	98	98	98	0.98	1.08	N
130	52	M	5	-	-	-	98	98	98	98	98	98	1.14	1.18	N
131	64	F	8	CKD	SHT	-	97	97	97	97	96	96	0.88	0.90	ATHEROMATOUS NARROWING +
132	44	M	7	-	-	-	98	98	97	97	97	97	1.06	0.98	N
133	47	F	3	-	-	-	98	98	98	98	98	98	1.20	1.24	N
134	70	M	10	CKD CAD DSPN	SHT	-	98	98	98	98	97	97	1.12	1.16	MONOPHASIC FLOW LT. PA, PTA
135	68	F	9	DSPN CAD	-	-	99	98	96	96	96	96	0.78	0.90	MONOPHASIC FLOW LT. DPA
136	56	M	7	CAD DR	SHT	Y	98	98	98	98	97	97	0.90	0.96	N
137	68	M	16	DSPN DR CAD	SHT	Y	98	98	96	96	95	95	0.76	0.90	MONOPHASIC FLOW RT. ATA, PTA, DPA
138	47	F	7	-	-	-	99	99	99	99	99	99	1.16	1.09	N
139	60	F	10	DSPN	SHT	-	98	98	98	97	97	97	0.94	0.90	N
140	63	M	10	CAD	SHT	Y	99	98	98	98	98	98	0.98	1.08	N
141	48	F	6	-	SHT	-	98	98	99	99	98	98	1.18	1.00	N
142	63	F	11	DSPN CAD	SHT	-	99	99	98	98	98	98	1.07	1.11	N

143	53	M	3	CAD	SHT	Y	97	98	97	98	97	97	1.04	1.00	N
144	55	M	5	-	-	-	99	99	99	99	98	98	1.01	1.19	N
145	60	M	4	-	SHT	Y	98	98	98	98	98	98	1.11	1.21	N
146	60	F	10	DSPN	SHT	-	98	98	98	97	97	97	0.94	0.90	N
147	56	M	10.5	DSPN CAD	SHT	Y	99	98	96	96	96	95	0.76	0.74	N
148	56	F	7	-	-	-	99	99	99	99	99	98	1.02	1.22	N

CONSENT FORM

PATIENT CONSENT FORM

Study detail:

""Usefulness of Pulse Oximetry and Ankle-brachial Index for screening Asymptomatic Peripheral vascular disease in Type 2 Diabetes mellitus."

Study centre : TERITIARY CARE CENTRE
Patients Name :
Patients Age :
Identification Number :

Patient may check (✓) these boxes

I confirm that I have understood the purpose of procedure for the above study. I have the opportunity to ask question and all my questions and doubts have been answered to my complete satisfaction. ☐

I understand that my participation in the study is voluntary and that I am free to withdraw at any time without giving reason, without my legal rights being affected. ☐

I understand that sponsor of the clinical study, others working on the sponsor's behalf, the ethical committee and the regulatory authorities will not need my permission to look at my health records, both in respect of current study and any further research that may be conducted in relation to it, even if I withdraw from the study I agree to this access. However, I understand that my identity will not be revealed in any information released to third parties or published, unless as required under the law. I agree not to restrict the use of any data or results that arise from this study. ☐

I agree to take part in the above study and to comply with the instructions given during the study and faithfully cooperate with the study team and to immediately inform the study staff if I suffer from any deterioration in my health or well-being or any unexpected or unusual symptoms. ☐

I hereby consent to participate in this study. ☐

I hereby give permission to undergo complete clinical examination and diagnostic tests including hematological, biochemical, radiological tests. ☐

Signature/thumb impression:

Patients Name and Address: place date

Signature of investigator :